HYPERAMYLAESEMIA AS AN INDICATOR OF SEVERITY AND PREDICTOR OF RESPIRATORY FAILURE IN ORGANOPHOSPHOROUS COMPOUND POISONING

By

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Dissertation submitted to the

SRI DEVARAJ URS ACADEMY OF HIGHER EDUCATION AND RESEARCH, KOLAR,KARNATAKA.

In partial fulfillment of the requirement for the degree of

DOCTOR OF MEDICINE (M.D.)

IN

GENERAL MEDICINE

Under the guidance of

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SRI DEVARAJ URS MEDICAL COLLEGE, KOLAR,

APRIL- 2018

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ACKNOWLEDGEMENT

I thank the almighty for showering his blessings on me.

I sincerely thank my respected teacher, **Dr. B.N.RAGHAVENDRA PRASAD** for his step-by-step guidance and constant extended support with the timely advices which helped me for this study.

I am deeply grateful to my co-guide **Dr. K.N.SHASHIDHAR ,** Professor & HOD, Department of biochemistry for his constant encouragement and rendered meticulous expert advice during the course of this study.

I thank **Dr.Prabhakar.k,** professor and HOD **, Dr. Lakshmaiah** and **Dr.P.N Venkatarathnamma,** and **Dr.Raveesha** professors ,Department of general medicine , for his constant guidance and advices.

I would like to thank **Dr.Harish kumar, Dr.Prasanna, Dr.Vidyasagar, Dr.Niveditha, Dr.Viswanath reddy**, Department of General medicine,for their constant support ,guidance and expert advice during the course of the study.

I express my gratitude to **Dr. S.R. Prasad** professor of microbiology and Director of post graduate studies for his encouragement and valuable inputs for the study.

To all my teachers throughout my life for having made me what I am today.

My deep felt gratitude to my dear parents and sister **MR.M.LOKESHWARA REDDY & MRS.RADHIKA, M.HARIKA SAI** whose countless sacrifices and blessings have made me who I am today.

I am also thankful to my postgraduate colleagues, seniors, juniors and friends for their constant motivation and countless help.

Last but not least, I thank all my patients involved in this study, without whose co-operation, this study would not have been possible.

Dr. M.MONICA SAI

ABSTRACT

BACKGROUND:

Organophosphate (OP) pesticide poisoning is a major challenging public-health problem in developing countries like Pakistan, Sri Lanka, India and other developing countries of Asia. OP compounds have been employed as pesticides, petroleum additives and chemical warfare nerve agents. The organophosphates have been used as pesticides for more than 50 years and are still used in most developing countries.

The OP compounds act by inhibiting acetylcholine esterase enzyme at nerve endings and neuromuscular junction, causing overstimulation of acetylcholine receptors. Signs and symptoms of poisoning are mainly due to muscarinic, nicotinic and central nervous system (CNS) receptor over-stimulation.

In laboratory assessment of OP poisoning, estimation of plasma cholinesterase is most specific test for OP poisoning. OP compound poisoning is associated with various biochemical abnormalities, among which hyperamylasemia is well documented.

It has been shown that OP compounds cause excessive cholinergic stimulation. This excessive cholinergic stimulation resulting in increased serum amylase which indirectly can assess the need for ventilatory support and severity of poisoning.

OBJECTIVES:

1.To estimate serum amylase levels in Organophosphorus compound poisoning

2. To correlate serum amylase levels with the severity of Organophosphorus compound poisoning by using Peradeniya Organophosphorus Poisoning (POP) scale.

3.To assess serum amylase levels in Organophosphorus compound poisoning as a need for ventilatory support.

MATERIAL AND METHODS:

Patient or the patient attenders were explained about the entire procedure and informed consent was taken in their own understandable language. Information is collected through a pre-tested proforma from each patient. A detailed history was collected from patient or from the patients relative or immediate bystander accompanying the patient.

Peradeniya Organophosphorus Poisoning scale was applied to all study subjects and the severity of Organophosphorus poisoning was graded as mild, moderate, severe at the time of admission.

3 ml of plain blood were collected from the outpatients on admission, serum amylase levels were estimated. Apart from serum amylase

other relevant and routine investigations were done .All the parameters were analyzed in Dry chemistry Vitros 250 Johnson and Johnson analyzer. During the analysis, regular and routine internal quality checks using Bio-Rad controls was carried out.

RESULTS:

A total of 98 cases satisfying the inclusion and exclusion criteria were studied. Out of 98 patients males were 60 (61.2%) and females were 38 (38.8%). 55 patients were in age group of 18 -30 years , 28 patients were in age group of 31-43 years,7 patients were in age group of 44-56 years,8 patients were in age group of 57-69 years .52 (52%) patients had normal serum amylase levels (<130 u/l) , 46(46.9%) patients had increased amylase levels (>130u/l).

58 (59.2%) patients in study had mild severity of poisoning, 20 (20.4%) patients had moderate severity of poisoning, 20 (20.4%) patients had severe poisoning. 45(45.9%) patients in the study had < 4850 serum pseudo cholinesterase levels,53 (54.1%) patients had >4850 pseudo cholinesterase levels. 31 patients with increased amylase levels had decreased pseudo cholinesterase levels. There was statistically significant (<0.05) association between serum amylase levels and pseudo cholinesterase.

17 patients with increased serum amylase levels (>130u/l) had severe pop score levels , whereas 3 patients with normal serum amylase (<130u/l) had severe pop score. There was statistical significance (<0.05) between serum amylase and pop score .35 patients with increased serum amylase (>130u/l) required ventilator support compared to 4 patients (<130u/l) with normal amylase levels and association was statistically significant (<0.05).

CONCLUSION:

Hyperamylasemia is common in OP poisoning, due to excessive cholinergic stimulation of pancreas. Amylase estimation can be used as a prognostic indicator along with the serum cholinesterase activity. Estimation of Serum amylase levels in OP compound poisoning will help in assessing severity of poisoning, and also need for ventilator support. It enables the early recognition of severity and also helps to identify those at risk of developing the complications of Organophosphorous poisoning. It also helped in identifying patients at risk of developing respiratory failure.

LIST OF ABBREVIATIONS USED

WHO - World Health Organization

WWII - World war II

OP - Organophosphorus

POP - Peradeniya organophosphorus Poisoning scale

RBC – Red blood cells

CNS - Central nervous system

DOPE - Delayed organophosphate encephalopathy

OPIDP - Organophosphate induced delayed polyneuropathy

QTc - Corrected QT interval

ACh – Acetylcholine

AchE - Acetyl cholinesterase

SchE – Serum cholinesterase

IMS - Intermediate syndrome

ENMG - Electroneuromyogram

FFP – Fresh Frozen Plasma

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INTRODUCTION

INTRODUCTION

Organophosphate (OP) pesticide poisoning is a major challenging public-health problem in developing countries such as India, Pakistan and Sri Lanka other developing countries of Asia[1].

Organophosphorus (OP) compounds have been employed as pesticides, petroleum additives and chemical warfare nerve agents. The organophosphates have been used as pesticides for more than 50 years and are still used in most developing countries. Organophosphorus pesticides poisoning can result from occupational, accidental or intentional exposure[1].

OP compounds are documented to have more adverse effects in developing countries such as India due to its easy availability and less awareness about its impact leading to high morbidity and mortality. The OP compounds act by inhibiting acetylcholine esterase enzyme at nerve endings and neuromuscular junction, causing overstimulation of acetylcholine receptors. Signs and symptoms of OP poisoning are mainly due to muscarinic, nicotinic and central nervous system (CNS) receptor over stimulation.

Acute poisoning by Organophosphorus pesticides (OP) has reached epidemic proportions in most parts of the world, particularly in developing countries such as India, where agriculture is the backbone. OP compounds ease to access and socio cultural factors play important role for Organophosphorus as a self-poison and the incidence is higher among young

economically active group with a common fatality ratio of 20%. In India, Organophosphorus compounds cause more self-poisoning deaths in southern and central India[4].

Laboratory evaluation plays an important and crucial role for confirmation of poisoning, diagnosing the first acute organ damage and assessing the severity of poisoning. In laboratory assessment of OP poisoning, estimation of plasma cholinesterase is most specific test for OP poisoning. OP compound poisoning is associated with various biochemical abnormalities, among which hyperamylasemia is well documented.

It has been shown that excessive cholinergic stimulation using an acetylcholine agonist can result in acute pancreatitis. Organophosphate used as an insecticide irreversibly inhibits cholinesterase resulting in delayed breakdown of synaptic acetylcholine and has been noted to cause acute pancreatitis in humans. This excessive cholinergic stimulation resulting in increased serum amylase which indirectly can assess the need for ventilatory support.

Respiratory failure is the most common complication of OP poisoning leading to death. Owing to limited availability of resources in India, it is important that clinical features and criteria to predict the need for ventilator support be identified at initial examination. Elevated serum amylase is also related to the development of respiratory failure in OP poisoning.

Estimating serum amylase levels in Organophosphorus compound poisoning is significant in assessing the severity of OP compound poisoning.

The Peradeniya Organophosphorus Poisoning (POP) scale assesses the severity of the poisoning based on the symptoms at presentation and is simple to use. The correlation may help in predicting the clinical outcome and in making timely decisions regarding transferring the patients for intensive care management.

OBJECTIVES

OBJECTIVES OF THE STUDY

1. To estimate serum amylase levels in Organophosphorus compound poisoning.
2. To correlate serum amylase levels with the severity of Organophosphorus compound poisoning by using Peradeniya Organophosphorus Poisoning (POP) scale.
3. To assess serum amylase levels in Organophosphorus compound poisoning as a need for ventilatory support.

REVIEW OF LITERATURE

REVIEW OF LITERATURE

History of Organophosphates:

Organophosphates were synthesized by von Hoffman. In 1873, he synthesized methyl phosphorus chloride, which led to the synthesis of a number of insecticides. Tetraethyl pyrophosphate was synthesized as the first OP cholinesterase inhibitor. During 1934–1944, Gerhard Schrader, a German chemist at Farben industries and his co-worker's synthesized about 2,000 OP compounds, including parathion as a pesticide and tabun, sarin, and soman as chemical warfare nerve agents. Although the nerve agents had been produced in Germany, they were not applied during World War II (WWII). At the end of WWII, the chemistry of OP compounds developed rapidly. Main use of nerve agents was reported during the Iran–Iraq war (1980–1988). These organophosphate compounds were re-purposed as insecticides after the war, and many organophosphate insecticides continue to be used today.

Epidemiology:

WHO estimates that three million cases of poisoning occur worldwide, mostly in the developing countries[4]. A Recent study from south India reported mortality rate of 4% in poisoning cases[5]. Organophosphorus pesticides poisoning can result from occupational, accidental or intentional

exposure. Mortality is higher in the developing countries where OP pesticides are readily available and may be used for suicide. Of the estimated 5,00,000 deaths from self-harm in the region each year about 60% are due to pesticide poisoning.. Many studies estimate that OP pesticides are responsible for around two-thirds of these deaths a total of 3,00,000 a year. 99% of cases occur in the developing world. Deaths from unintentional OP poisoning are less common than those from intentional poisoning and seem to be more common in regions where highly toxic OP pesticides (WHO Class I toxicity) are available**.**

Chemistry and classification of OP compound poisoning:

Organophosphorus (OP) compounds refer to any group of organic chemicals that contain phosphorus. The most predominant valances of phosphorus are 3 and 5. The majority of OP compounds (OPs) with environmental and industrial applications are of the pentavalent types. Organophosphates are a significant group of OPs which are essentially esters of phosphoric acids, in which the nature of the substituents attached to phosphorus plays a key role in determining the toxicity of the agents.

The commonly used OP insecticides are acephate, anilophos, chlorpyrifos, dichlorvos, diazinon, dimethoate, fenitrothion,

Methyl parathion, monocrotophos, phenthoate, phorate, pirimiphos, quinalphos, temephos, etc.

The replacement of an oxygen atom in Organophosphorus structure by sulfur leads to the formation of organothiophosphorus compounds such as malathion and parathion, which have a lower lethal potential but *in vivo* metabolization to the axon metabolite enhances their toxicity **.**

Organophosphates can be divided into two types: diethyl (e.g. chlorpyrifos, diazinon, parathion, phorate and dichlofenthion) and dimethyl (e.g. dimethoate, dichlorvos, fenitrothion, Malathion and fenthion).

Classification of OP compounds:

Table 1:

Group	**Compounds**
Nerve agents	Tabun ,Sarin, Soman
Diethyl	Chlorpyrifos, Diazinon, Parathion, Phorate ,Dichlorfenthion, Quinalphos
Dimethyl	Dimethoate, Dichlorvos, Fenitrothion, Malathion and Fenthion.
others	Profenofos, Monocrotophos, Acephate, Thiamate, methamidophos

Classification of OP compounds based on their toxicity

Table 2:

High toxicity	Moderate toxicity	Less toxicity
Monocrotophos Profenofos parathion	Dimethoate Quinalphos Chlorpyrifos Fenthion	Malathion

Pathophysiology:

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

Normally the cholinesterases rapidly hydrolyze the neurotransmitter acetylcholine into inactive fragments of choline and acetic acid after the completion of neurochemical transmission. The neurotransmitter acetylcholine is present in the terminal endings of all postganglionic parasympathetic nerves, at myoneural junctions, and at both parasympathetic and sympathetic ganglia.

The major toxicity of organophosphate compounds is the covalent binding of phosphate radicals to the active sites of the cholinesterases, transforming them into enzymatically inert proteins[2].

Organophosphates act as irreversible cholinesterase inhibitors because the organophosphate-cholinesterase bond is not spontaneously reversible without pharmacological intervention. The inhibition of cholinesterase activity leads to the accumulation of acetylcholine at synapses, causing overstimulation and subsequent disruption of transmission in both the central and peripheral nervous systems. Exposure to organophosphate compounds will, therefore, interfere with synaptic transmission peripherally at muscarinic neuroeffector junctions and nicotinic receptors within sympathetic ganglia and at skeletal myoneural junctions. This is accomplished by an overstimulation of acetylcholine receptor sites that leads to a variety of physiologic and metabolic derangements. Disruption of transmission also will occur at the acetylcholine receptor sites within the central nervous system.

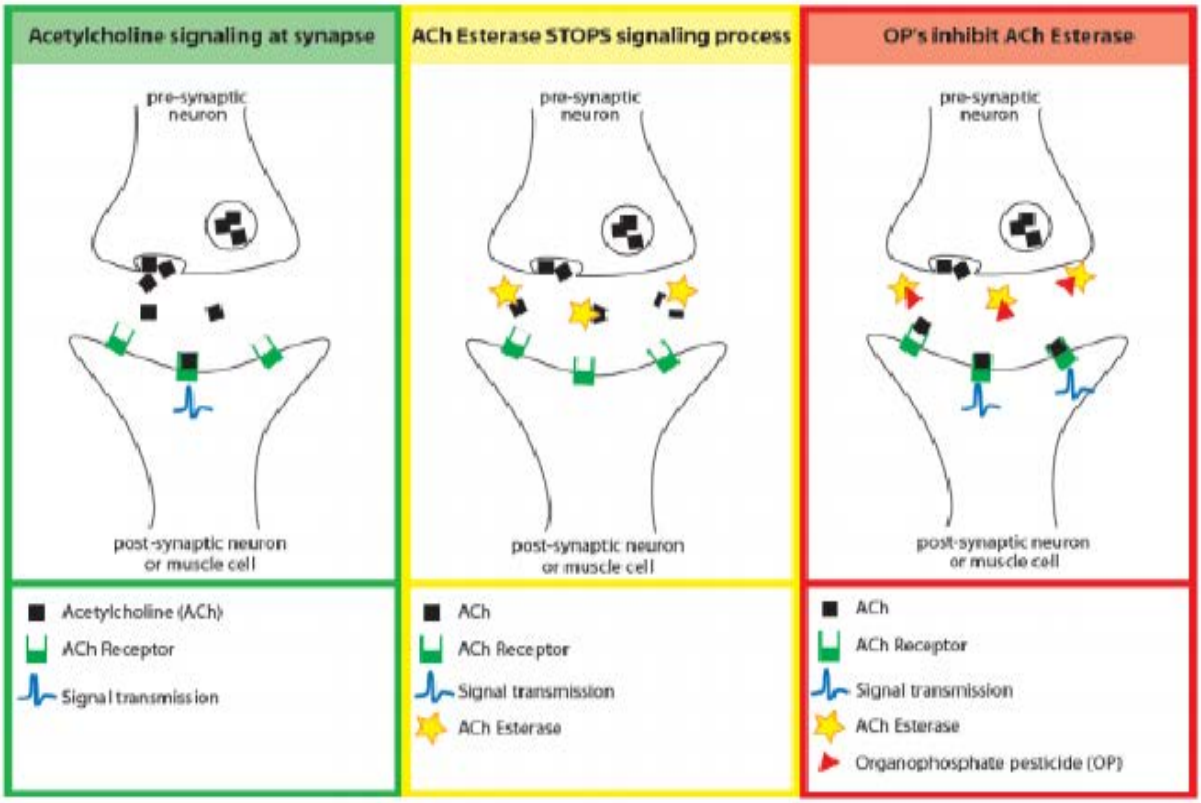

Figure 1 showing Mechanism of op compounds inhibiting AchE

OP COMPOUNDS (inhibition of enzyme AchE)

↓

AchE

Acetylcholine ⟶ Acetic acid + Choline

Accumulation of AChE ⟶ occurrence of nicotinic, muscarinic and central

Effects.

Table 3 showing mechanism of op compound poisoning

CLINICAL MANIFESTATIONS:

Signs and symptoms of acute organophosphate poisoning according to receptor site involved shown in Table 4:

Nicotinic	***Muscarinic***	***Central effects***
Tachycardia, Hypotension, Weakness, Fasciculations, Cramps, Paralysis	Bradycardia, Hypotension Rhinorrhea, Bronchorrhea Bronchospasm, Cough, Nausea, Vomiting, Abdominal pain, Diarrhea, Fecal incontinence, Blurred Vision Increased Lacrimation, Miosis, Excessive sweating Increased Salivation, Urinary incontinence.	Anxiety, Restlessness, Ataxia, Absent reflexes, Convulsions, Insomnia, Tremors, Dysarthria, Coma, Hyperreflexia, Respiratory depression, Circulatory collapse

Symptoms based on time of occurrence

The time of occurrence of symptoms and signs depend on the route of exposure, poison load and chemical nature and solubility characteristics of the compound. Traditionally, symptoms are categorized as acute (minutes to hours) and delayed or late (days to weeks). The time of onset and mechanism of delayed manifestations such as intermediate syndrome, delayed onset coma and extrapyramidal manifestation[32] are different to that of late manifestations such as organophosphate induced delayed polyneuropathy (OPIDP) that typically occurs after 2-3 weeks and up to 4-week post exposure. Thus, we propose that symptom onset is categorized as acute (within 24-h), delayed (24-h to 2-week) and late (beyond 2-week).

Acute onset symptoms

The acute symptoms and signs are due to muscarinic, nicotinic and central receptor effects. Muscarinic symptoms of salivation and bronchorrhea that dominate initially may cause drowsy patients to drown in their secretions. Acute muscarinic effects on the heart (bradycardia, hypotension) can be life-threatening. Nicotinic effects of muscle weakness contribute to respiratory distress whilst the acute central effects of restlessness, agitation, confusion and sometimes convulsions further compromise airway and breathing and increase aspiration risk and hypoxia.

Since many of these effects are reversed by atropine, early and appropriate medical attention is vital. In developing countries, where OP poisoning is common, quick access to medical care is more problematic than early recognition[33].

Delayed onset symptoms

With adequate atropinization, the acute cholinergic symptoms abate within a few hours, but some patients develop delayed effects. Although acute cholinergic manifestations typically occur within 24-h of exposure, late onset cholinergic symptoms and signs have been observed 40-48 h after dichlofenthion poisoning.

Intermediate syndrome, the best described delayed manifestation, is characterized by paralysis of proximal limb muscles, neck flexors, motor cranial nerves and respiratory muscles 24-96 h after poisoning, after the cholinergic phase had settled down, with weakness lasting for up to 18-day. A neuromuscular junctional defect has been demonstrated in electromyography studies. Delayed onset intermediate syndrome has been reported 114-h after methamidophos poisoning. Since methamidophos is highly lipophilic and persists in fat stores, re-distribution

and re-inhibition of cholinesterase may have delayed symptom onset[35]. Although intermediate syndrome involves muscle groups, focal weakness has also been reported; in particular, laryngeal paralysis, either acute or delayed by 4-14 days presenting as "failed extubation". Laryngeal electromyography was consistent with bilateral laryngeal paralysis although standard needle electromyography was normal. Severe and prolonged diaphragmatic paralysis has also been reported with Malathion poisoning[34]. Coma is seen in 17-29% of patients and can last for hours to days. OP poisoning may also present as brainstem stroke. Some patients manifest altered consciousness or coma days after poisoning, particular after a period of "normal" consciousness. This clinical entity termed**delayed organophosphate encephalopathy (DOPE) or "CNS intermediate"** is probably akin to type II paralysis. Coma with absent brainstem reflexes or encephalopathy has been reported after 4-day of normal consciousness and spontaneously resolved after another 4-day. The clinical distinguishing feature between "brain death" and this "mimic" was "small miosed pupils" in patients with DOPE. Delay in coma onset was attributed to the slow release and re-distribution of the lipid soluble OP compounds with saturation of the CNS receptors over time rather than immediately[36,37].

Late onset symptoms

The classical late onset neuropathy in OP poisoning, OPIDP is characterized by distal weakness that occurs 2-4 weeks after OP exposure. The molecular target for OPIDP is considered to be the neuropathy target esterase which is inhibited by OPs. Electrophysiological changes include reduced amplitude of the compound muscle potential, increased distal latencies and normal or slightly reduced nerve conduction velocities[38, 39]. Nerve biopsy may show features of axonal degeneration with secondary demyelination. Recovery is, usually, complete, particularly in the young. However, mild weakness with increase in vibration threshold may persist for 2-year following acute poisoning. Other late onset features reported include cerebellar ataxia, developing about 5-week after acute exposure to an OP [and] extrapyramidal symptoms at 40-day[40].

Clinical features of OP compound poisoning based on time of occurrence

Table 5:

Time of manifestation	Mechanism	Manifestation
Acute (mts – 24 hrs)	Nicotinic receptor action	Weakness, fasciculation, cramps, paralysis.
	Muscarinic receptor action	Salivation, lacrimation, urination, defecation, emesis, bradycardia, hypotension, miosis.
	Central	Anxiety, Restlessness, respiratory depression, convulsions
Delayed (24hrs-2 weeks)	Nicotinic receptor action	Intermediate syndrome
	Muscarinic receptor action	Cholinergic symptoms like bradycardia, miosis, salivation
	central	Coma, extrapyramidal symptoms
Late (2-4 weeks)	Peripheral neuropathy target esterase	Organophosphate induced delayed polyneuropathy

Organ specific manifestations

An organ specific approach enables focused attention and support of specific organ dysfunction. Given that OP compounds are neurotoxic insecticides, the dominant organ involved in acute and chronic exposure is the nervous system.

Neurological manifestations

Three types of paralysis are described. Type I paralysis, characterized by weakness, fasciculations, cramps and twitching, occurs acutely with the cholinergic symptoms. Type II paralysis, seen in 80-49%, occurs more insidiously 24-96 h following poisoning and has a predilection to proximal, neck and respiratory muscles and cranial nerves with recovery in 1-2 weeks. Type III paralysis characterized by distal weakness occurs 2-3 weeks after poisoning with recovery in weeks to months. Weakness of specific muscle groups at sites of dermal exposure, cranial nerve palsies, supra nuclear gaze palsy, isolated laryngeal paralysis and diaphragmatic paralysis are all reported[42,43].

Restlessness, delirium, agitation, convulsions or coma may occur with acute exposure while neuropsychiatric symptoms and signs termed chronic organophosphate induced neuropsychiatric disorder may occur with chronic

exposure. Extrapyramidal manifestations, ocular signs, ototoxicity, presentation as a Guillain-Barre syndrome and sphincter involvement are also described.

Cardiovascular manifestations

Cardiac manifestations are observed in about two-thirds of patients with OP poisoning .Common electrocardiographic findings are QTc prolongation, ST-T segment changes and T wave abnormalities. Other cardiac manifestations include sinus bradycardia or tachycardia, hypotension or hypertension, supraventricular and ventricular arrhythmias and ventricular premature complexes and noncardiogenic pulmonary edema[45].

Death due to cardiac causes in OP poisoning occurs either due to arrhythmias or severe and refractory hypotension. Although shock is primarily vasodilatory, circumferential endocardial ischemia with cardiogenic shock and leading to death has also been reported with Malathion poisoning. Necropsy of patients who died following OP poisoning has revealed cardiac discoloration or blotchiness, patchy pericarditis, auricular thrombus and right ventricular hypertrophy and dilatation[46]. Myocardial interstitial edema, vascular congestion, patchy interstitial inflammation, mural thrombus and patchy myocarditis were the histological

findings. OP poisoning presenting as cardiac arrest and late onset, prolonged asystole 12-day following poisoning have been described[47].

Respiratory symptoms

Respiratory symptoms are common in OP poisoning. Muscarinic effects of salivation, rhinorrhea, bronchorrhea and bronchospasm contributed to hypoxemia and increased work of breathing. Nicotinic effects result in muscle weakness and paralysis and predispose to hypercapnic respiratory failure. Central effects of agitation, restlessness and seizures further compromise respiratory function[48].

In large cohorts, respiratory failure is reported to occur in 24-66% of patients. Severity of poisoning was the primary determinant of respiratory failure. Other factors contributing to respiratory failure include pneumonia, cardiovascular collapse, acute pulmonary edema and acute respiratory distress syndrome[49,50].

The mechanism of respiratory failure has been explored in experimental models. As described earlier, OP compounds cause excitatory changes in the respiratory control regions with an initial increase in phrenic nerve output and subsequent sudden cessation of activity. More recently, in a rodent model, exposure to dichlorvos caused a rapid lethal central apnea that

was potentiated by hypoxia and protected by vagally mediated feedback signals[51].In animals sustained with mechanical ventilation, following central apnea, there was progressive pulmonary insufficiency. Brief central apnea and complete acetylcholinesterase inhibition of the brainstem has also been reported with crotylsarin, another OP compound. In other studies, paraoxon failed to produce apnea in a rat model, although postinjection and throughout the study, there was a significant decrease in the respiratory frequency and a significant increase in the expiratory time without modifications in the inspiratory time[52].

Other features

Gastrointestinal symptoms occur early in OP poisoning and are rapidly reversed with atropine therapy. There are concerns that atropine slows down intestinal transit time and prolongs OP toxicity. In one series, persistence of the OP in the gut was demonstrated 10-day after poisoning. Atropine therapy may also preclude early enteral feeding in OP poisoned patients. However, in a pilot study, early administration (by 48-h) of hypocaloric feeds was associated with gastric stasis in only 6.9% of patients receiving enteral feeds. Pancreatitis is not uncommon in OP poisoning and reported in 12.8%. Metabolic complications such as hyperglycemia and glycosuria and OP intoxication presenting as diabetic ketoacidosis are also described[53].

Implications of route of exposure on onset of symptoms

The route of exposure determines the rapidity of symptom onset. Common routes of exposure are inhalational, skin and ingestional. The inhalational route has the fastest onset, generally within a few minutes of exposure. In the terrorist attacks in Japan with the nerve gas agent Sarin, instantaneous death by respiratory arrest was suggested in 4 victims. In farmers, inhalation exposure resulting in rapid symptom onset may occur with a sudden change in the wind direction during insecticide spraying[54].

In skin exposure, the volume of exposure, intactness of the skin and solubility characteristics of the OP determines lag-time. In one report, nausea, abdominal cramping, arm and leg weakness occurred within 30-min of dermal exposure of chlorpyrifos, a lipid soluble OP. Although leg weakness improved, weakness of muscles at the site of skin exposure persisted beyond 2-week. In another report, symptom onset occurred at 3-h following the exposure to water soluble OP, monocrotophos, through a skin laceration.] Symptoms of poisoning have also occurred after 4-h and 24-h after application of a home-made shampoo contaminated with an OP. In a rare situation of subcutaneous chlorpyrifos self-injection, delayed cholinergic phase, prolonged coma and severe permanent neurologic injury were observed. Delayed and prolonged effects were attributed to the adipose and muscle tissue acting as reservoirs[55].

In ingestional poisoning, symptom onset would depend on the poison load and absorption characteristics. In general, symptoms occur within a few minutes to hours. However, the first symptom in parathion poisoning may be delayed by up to 24-h as parathion must first be converted from the thion to the oxon form to be physiologically active[56]. Many organothiophosphates readily undergo conversion from thions to oxons. This conversion occurs due to the substitution of oxygen for sulfur in the environment under the influence of oxygen and light, and in the body chiefly by the action of liver microsomes. Oxons are generally more toxic than thions, but axons break down more readily.

DIAGNOSIS

It is based on-

1. H/O ingestion of the OPC.
2. Characteristic clinical features.
3. Clinical improvement after atropine and oxime therapy.
4. Inhibition of cholinesterase activity.

1.Inhibition of cholinesterase activity - (RBC or true cholinesterase and plasma or pseudocholinesterase)

The definitive and the gold standard method in the diagnosis of OPC poisoning is established by demonstrating a decreased cholinesterase in the blood. Theoretically, RBC or true cholinesterase is a more accurate test compared to serum or butyryl or pseudocholinesterase; but the serum cholinesterase (SChE) is more readily available and measured in most labs, easier to assay and more useful in acute exposure. Ideally, the diagnosis of OPC poisoning is based on a drop of 50% of normal value of cholinesterase from the baseline[58]. Since most patients don't have baseline values, the diagnosis can be confirmed by a progressive increase in cholinesterase value with treatment. Mild poisoning is defined as cholinesterase of 20-50%, moderate 10-20% and severe<10% of normal enzymatic activity. It is to be noted that unfortunately many labs don't have the in-house capability to run the cholinesterase levels[57]. So it is important that any patient presenting with full-blown cholinergic syndrome should be treated empirically without waiting for the lab confirmation of decreased cholinesterase activity. Another important use of cholinesterase (serum) is in the monitoring the clinical course of the patients with the poisoning. A low cholinesterase is a predictor of IMS[59].

2. **Electroneuromyogram (ENMG) Studies:** Out of the various electro diagnostic abnormalities, the 30 Hz rapid nerve stimulation decremental

Response correlates best with clinically detectable weakness and hence it is the most useful diagnostic test for IMS[61,62].

3. Other investigations of prognostic significance in acute OPC poisoning are neutrophillic leucocytosis, hyperglycemia, proteinuria, ECG changes (QTc prolongation) , glycosuria, hyperamylasemia, blood PH[60].

Different management strategies used in the OP poisoning:

Management of OP poisoning is still a great challenge to the treating physician and is always associated with high morbidity and mortality particularly in developing countries. Current treatment practices mainly focused on gastrointestinal decontamination followed by administration of atropine and oximes as antidotes. The general management mainly aims to control the symptoms and reverse the effect of the OP compound.

Gastrointestinal decontamination

Gastric lavage and activated charcoal are most commonly used in gastrointestinal decontamination. Gastric lavage is the first intervention and most common form of decontamination for OP poisoned patient at the initial stages. Guidelines are suggest that lavage should be considered only if the patient arrives within1 hour of ingesting the poison. The relevance of these

guidelines with respect to OP poisoning is unclear. Gastric lavage should be considered for patients who present soon after ingestion of a substantial amount of toxic pesticide who are intubated, or conscious and willing to cooperate[43].

Activated charcoal can also be used in the treatment of OP poisoning if the patient is cooperative or intubated. It can be administered as a single dose or in multiple doses if the patient presents to the hospital within 1-2 hours of ingestion or in cases of severe toxicity. 1gram/kg of activated charcoal can be given orally via nasogastric tube at the end of the lavage. A randomized controlled trial of single and multiple doses of super activated charcoal in Sri Lanka failed to find a significant benefit of either regimen over placebo after testing in more than 1000 patients poisoned with pesticides[61,62].

Role of different Antidotes in OP poisoning

Atropine and oximes are the most commonly used antidotes in the management of poisoning. Recently the addition of Glycopyrrolate was found to be beneficial in the management of OP poisoning. It is administered along with atropine and reduces the total atropine requirement in the patient.

Atropine:

Anticholinergics are still the mainstay of treatment in acute OP poisoning and should be started as soon as the airway has been secured. Atropine will probably remain the drug of choice because it is available widely, is affordable, and is moderately able to penetrate the CNS[64]. It has only antimuscarinic action, but has no effect on nicotinic receptors. No known randomized controlled trials have compared different regimens of atropine for either loading or continuation therapy.

A 2004 review identified more than 30 dosing regimens of atropine, some of which would take many hours to obtain the full loading dose of atropine. The aim of early atropine therapy is to reverse cholinergic features and to improve cardiac and respiratory function as quickly as possible. The target end-points for atropine therapy are clear chest on auscultation, heart rate>80/min, systolic BP >80mmHg, pupils no longer pinpoint, dry axillae. The recommended dose of atropine varies from patient to patient till target end point is reached[67].

One dosage regimen says atropine is started initially as a 2-mg intravenous (IV) bolus and then at doses of 2-5 mg IV bolus every 5-15 minutes until atropinization is achieved. In another dosage regimen, an initial bolus of 1-2mg is recommended with subsequent doses doubled every 5 minutes until atropinization is achieved. This regimen requires not more than 20 minutes to administer 25mg of atropine[65]. It was found to be effective and

the most appropriate therapy for OP poisoned patients who need a large dose of atropine and it also works well for patients who need even low doses of atropine as low as 1mg.29 Similarly a study conducted in South India recorded the benefit of an atropine infusion compared with repeated bolus doses, but the drawback of this study was that it used historical controls which reduced the confidence in this finding. Continuous infusion reduced the blood level fluctuation of atropine when compared to bolus dose[66].

The markers used to detect atropine toxicity are – confusion, pyrexia, absent bowel sounds and urinary retention. The most common cause of respiratory failure and mortality in the early period of poisoning (usually < 48 hours) is inadequate atropinization[70].

Sl.no	vitals
1	Time
2	Heart rate
3	Pupils –size
4	Clear lung
5	Dry axilla
6	Bowel sounds
7	confused
8	temperature
9	Neck muscle weakness
10	Atropine infusion
11	Bolus given

Table 6 : vitals to be monitored during atropine therapy

Oximes:

Oximes are nucleophilic agents that are known to reactivate the phosphorylated acetylcholinesterase by binding to the OP molecule. Pralidoxime is the most common and widely used oxime. Use of oximes in OP poisoning remains conflicting and controversial[67]. It is more effective when it is administered immediately after exposure. However, in some cases it was found more effective in patients who presented late, even 2 to 6 days after exposure. WHO recommends an initial bolus of at least 30 milligrams/kilogram followed by an infusion of more than 8 milligrams/kilogram/hour. In some cases it can be given as an intermittent dosing with 1 to 2 grams diluted in 100 milliliters of normal saline infused over 15 to 30 minutes[68]. The dosing may be repeated at one hour after the initial dose if muscle weakness or fasciculation's are not relieved. The dose can be repeated at 3 to 8 hour intervals. The maximum dose in a day should not exceed 24grams.

Role of Pralidoxime in organophosphorus poisoning

The principal pharmacological effect of Pralidoxime is reactivation of cholinesterase which has been inactivated by phosphorylation as a result of exposure to organophosphates. Pralidoxime removes the phosphoryl group from the active site of the inhibited enzyme by nucleophilic attack and regenerates active cholinesterase forming a soluble complex with oximes.

Pralidoxime also detoxifies certain OPs by direct chemical reaction and probably also reacts directly with cholinesterase to protect it from inhibition[69]. Pralidoxime must be administered before aging of them inhibited enzyme. After aging is completed, phosphorylated cholinesterase cannot be reactivated. Pralidoxime does not equally antagonize all anticholinesterases because the aging of the inhibited enzyme varies and it mainly depends on the specific organophosphate bound to the cholinesterase. Pralidoxime also reactivates the cholinesterase inhibited by the carbamates which is having a faster reactivation than the phosphorylated compounds. The reactivation of anticholinesterase mainly occurs at the neuromuscular junction and there by inhibition of paralysis of respiratory and other skeletal muscles

Glycopyrrolate:

Glycopyrrolate has also been tried as an alternative for atropine. It is a quaternary ammonium anti-cholinergic agent, with anti-muscarinic activity with high selectivity for peripheral cholinergic sites like atropine and has been suggested as a useful drug in organophosphate intoxication for controlling secretions with minimal side-effects of flushing, tachycardia, and depressed level of consciousness often experienced with atropine. Glycopyrrolate has the advantages of better secretion control, less tachycardia and inability to cross the blood-brain barrier but it is less

effective in treating bradycardia and may not affect central neurological effects from organophosphates.61 A randomized control trial was carried out to compare the effects of atropine and Glycopyrrolate on 44 OP poisoned patients and 39 patients were evaluated (22 atropine and 17 Glycopyrrolate cases). The outcome was same in both the groups like Fatalities, need for ventilation etc.

Ventilatory support:

It is indicated in stupor/coma, hypoxemia with PaO2<60mmhg and Profound muscle weakness. Ventilatory support may be needed for respiratory Failure due to early acute cholinergic crisis (<24 hrs.) and late intermediate syndrome (>24 hrs.). In some cases, early intubation may lend to prolonged Ventilatory support.

The predictors for the need of ventilator support would be:

1. Delay in the initiation of specific treatment.
2. Low level of sensorium at admission
3. Pinpoint pupils and generalized fasciculation's.
4. Presence of convulsions
5. Presence of respiratory failure at admission.
6. High initial atropine requirement for atropinization

Role of other experimental therapies in management of OP poisoning

Benzodiazepines

Patients poisoned with OP frequently develop agitated delirium and some patients also develop seizures. Diazepam is the first-line therapy and it is used to reduce the agitation in OP poisoning. Diazepam is given at a dose of 10 mg by slow IV push and repeated as necessary up to 30–40 mg per 24 hours. Diazepam is preferred over haloperidol because of high doses of haloperidol may be needed for the patients receiving the atropine[72].

Magnesium Sulphate

No systematic review or randomized clinical trials, or observational studies of sufficient quality are available to prove benefit of magnesium sulphate in OP poisoning. Magnesium sulphate is an inhibitor of acetylcholine release in the central nervous system and at peripheral sympathetic and parasympathetic synapses. The use of magnesium in acute OP poisoning in humans has been reported in two small studies[74].

Sodium bicarbonate

Alkalization of the serum to pH 7.5 with sodium bicarbonate may be useful in the management of OP poisoning. Clinicians in Iran reported the successful management of OP-intoxicated patients using infusions of sodium bicarbonate. A Cochrane review concluded that insufficient evidence exists

at present to establish whether sodium bicarbonate should be used in humans poisoned with OP compounds[73].

Clonidine

The alpha2-adrenergic receptor agonist clonidine also reduces acetylcholine synthesis and release from presynaptic terminals. Animal studies show the beneficial effect of clonidine treatment, in combination with atropine and effects in human still not known[75].

Fresh frozen plasma(FFP)

Use of FFP in people with OP poisoning is that it may reduce high blood pesticide concentrations by increasing levels of butyrylcholinesterase. Butyrylcholinesterase is generally sensitive to OP pesticides and it is rapidly used up in moderate to severe poisoning. Replacement of butyrylcholinesterase can possible by administration of fresh frozen plasma or by plasmapheresis[76]. This will increase the level of enzyme in the blood and neutralize some pesticide. But increase in the level of butyrylcholinesterase enzymes and its clinical significance is not clear. A small controlled study which compared two arms, one arm treated with plasma (n=12) and other arm without plasma (n=21) showed benefit with fresh frozen plasma. But it was not a randomized trial and allocation of decisions was unclear[77].

METHODOLOGY

METHOD OF COLLECTION OF DATA:

Patient or the patient attenders were explained about the entire procedure and informed consent was taken in their own understandable language. Information is collected through a pre-tested proforma from each patient. A detailed history was collected from patient or from the patient's relative or immediate bystander accompanying the patient. Qualifying patients were subjected for a clinical examination and relevant biochemical investigations.

A thorough clinical examination was carried out with particular reference to vital parameters, pupil size, assessment of central nervous system, respiratory system, cardiovascular system as per prescribed proforma. Peradeniya Organophosphorus poisoning scale was applied to all study subjects and the severity of Organophosphorus poisoning was graded as mild, moderate, severe at the time of admission.

3 ml of plain blood were collected from the outpatients on admission, Blood was allowed to clot, serum was separated by centrifugation and used for the analysis of following parameters. Serum amylase levels were estimated. Apart from serum amylase other relevant and routine investigations were done.

Serum amylase levels were estimated by chromogenic method using dyed amylopectin. Estimation of plasma cholinesterase activity by kinetic method based on hydrolysis of butyrylthiocholine by choline esterase[2].

All the parameters were analyzed in Dry chemistry Vitros 250 Johnson and Johnson analyzer. During the analysis, regular and routine internal quality checks using Bio-Rad controls was carried out[80].

Quality control samples were supplied by BIO-RAD USA. IQAS values were considered considering 1-2S rule.

Figure 2 : vitro 250 drychemistry analyzer

SL.NO	PARAMETERS	SCORE
1	Miosis- Pupil > 2mm Pupil ≤ 2mm Pupils pin point	 0 1 2
2	Fasciculations- none Present but not generalized or continuous Generalised and continuous 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 ≤ 60/min	 0 1 2
5	Level of consciousness – Conscious and rational Impaired, responds to verbal commands Impaired, no response to verbal commands (if convulsion present add 1)	 0 1 2
	TOTAL	11

Table 7: POP score used for assessing severity of OP poisoning

INCLUSION CRITERIA:

1. Patients aged above 18 years.
2. Patients with history of ingestion, inhalation or cutaneous absorption of organophosphate compound within 24 hours.

EXCLUSION CRITERIA:

1. Patients with indication of exposure to an entirely different poison other than Organophosphorus poison.
2. Patients with Organophosphorous poisoning and mixed with any other poison.
3. Patients with Organophosphorous poisoning on mechanical ventilation.
4. Patients who have consumed poison along with alcohol/chronic alcoholics.
5. Patients with history suggestive of gall stone disease.
6. History suggestive of parotid gland disease.
7. Patients with history of lipid disorders.
8. Patients with history of renal or hepatic disease.
9. History suggestive of hyperparathyroidism.

10. Drugs likely to cause hyperamylasemia- mercaptopurine, thiazides , frusemide, pentamidine, opiates, azathioprine, asperginase, asprin, birth control pills, Cholinergic medications, Ethacrynic acid & Methyldopa.

RESULTS

RESULTS

A total of 98 organophosphorus compound poisoning patients satisfying the inclusion and exclusion criteria were taken up for study.

Gender distribution:

Gender	Frequency	Percent
female	38	38.8
male	60	61.2
Total	98	100.0

Table 8 : Gender frequency distribution

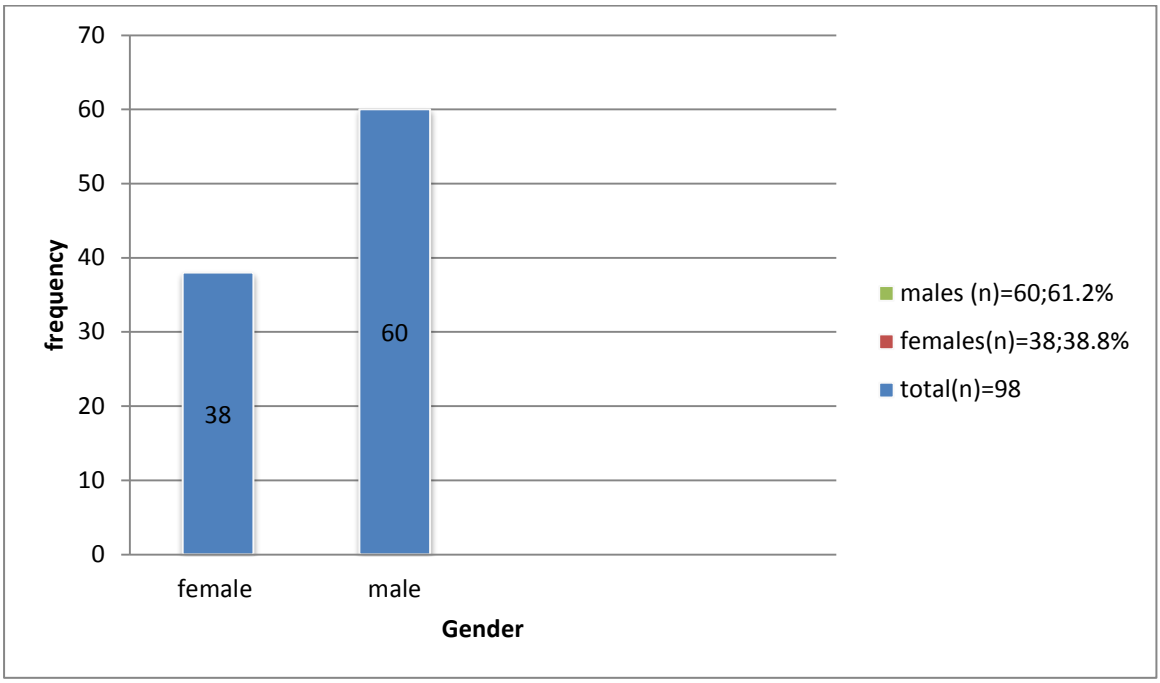

Figure 3 : Gender distribution in OP compound poisoning

N=98 patients; Males =60 (61.2%) ;Females =38 (38.8%)

Manner of poisoning:

Mode of poisoning	No of patients	percentage
Accidental	6	6.12%
Homicidal	2	2.04%
Suicidal	90	91.8%
Total	98	100%

Table 9 :Manner of poisoning

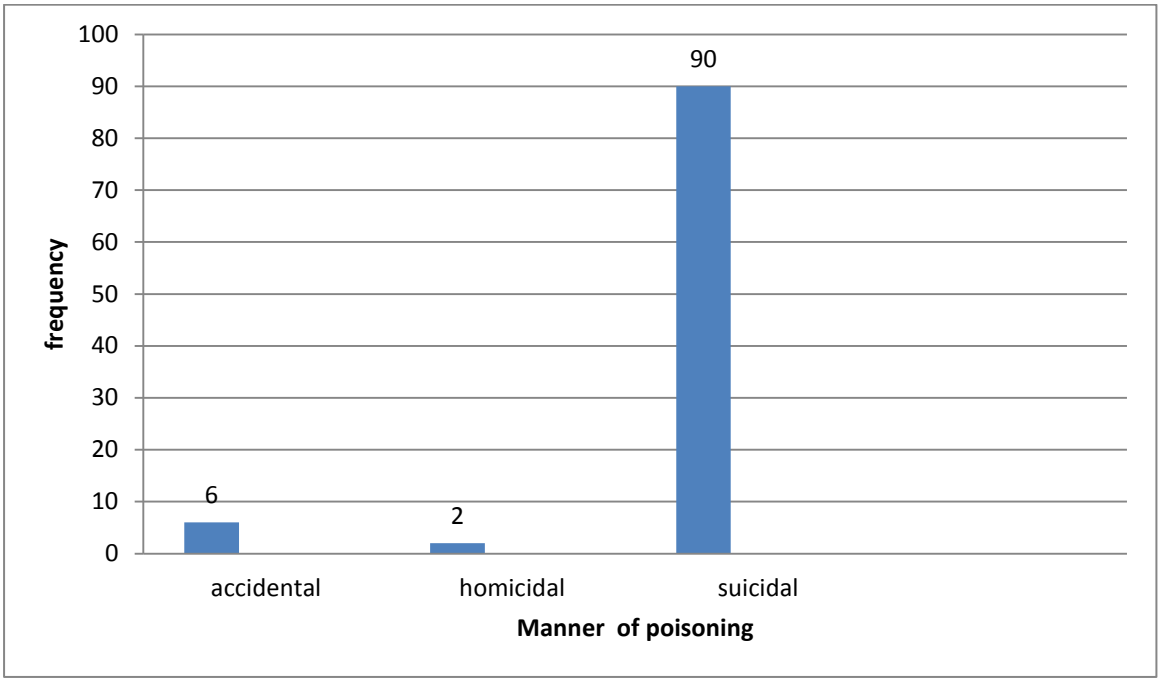

Figure 4 : frequency distribution of manner of poisoning

The most common manner for poisoning was suicidal-90 (91.8%) followed by accidental – 6(6.12%) and homicidal- 2(2.04%).

Age frequency distribution :

Age group	Frequency	Percent
18-30	55	56.12
31-43	26	26.53
44-56	5	5.1
57-69	12	12.24
Total	98	100.0

Table 10: age group distribution and its percentage

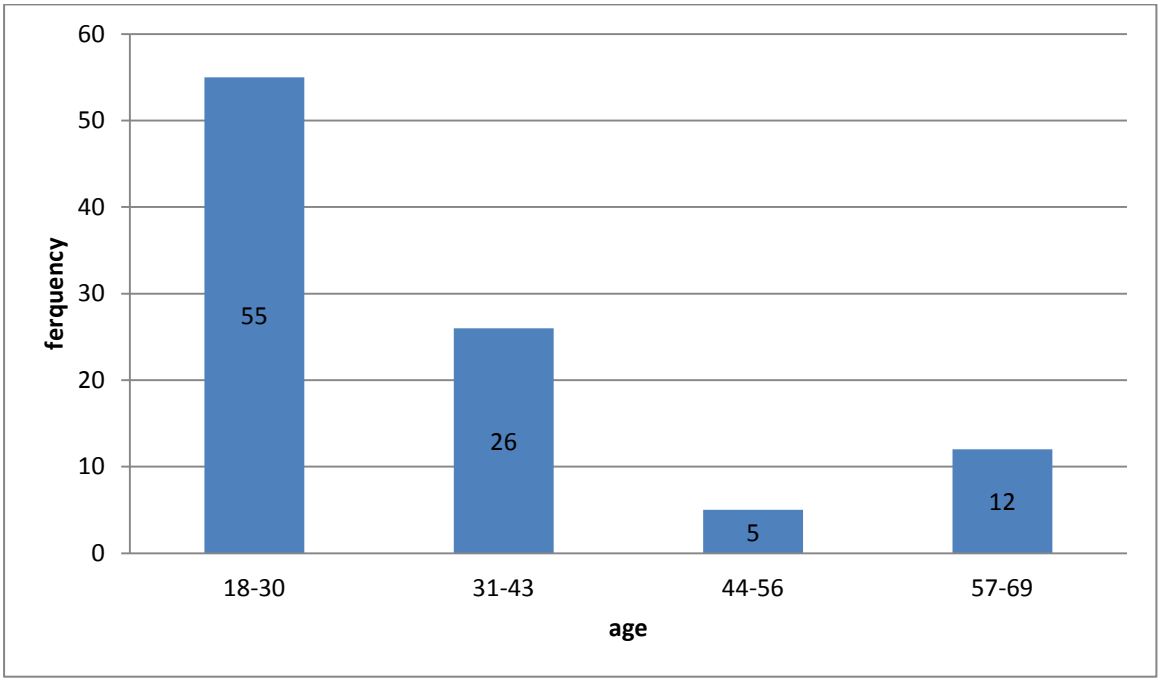

Figure 5 : age frequency distribution chart

- 55 patients were in age group of 18 -30 years ,
- 28 patients were in age group of 31-43 years,
- 7 patients were in age group of 44-56 years,
- 8 patients were in age group of 57-69 years

Clinical presentation:

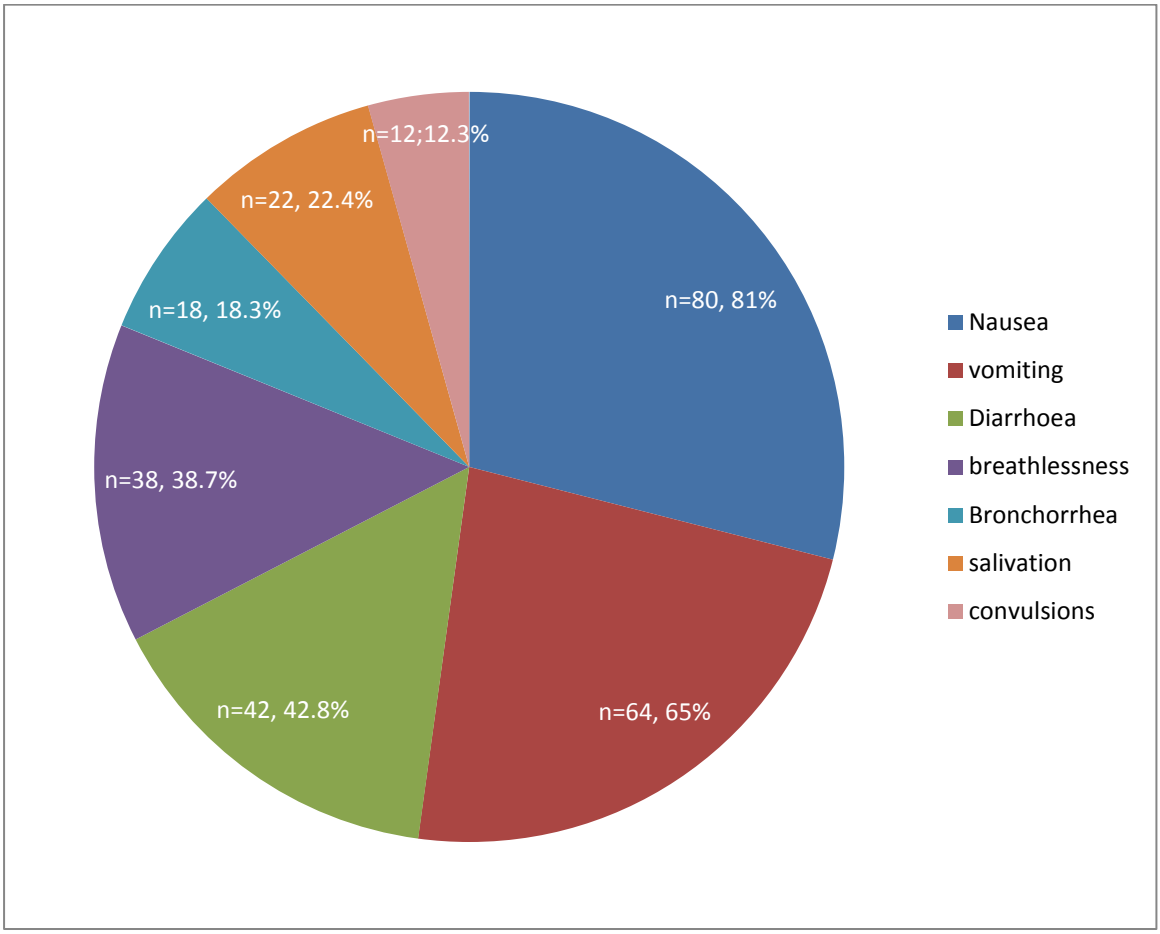

Figure 6: frequency of different clinical features in OP compound poisoning

The most common presentation was nausea which was seen in 80 (81%) of patients, followed by vomiting in 64 (65%), diarrhoea in 42(42.8%) ,breathlessness in 38 (38.7%), bronchorrhea in18 (18.3%),salivation in 22(22.4%),convulsions in 12(12.3%) of patients

Serum amylase distribution:

Amylase levels		Frequency	Percent
Valid	<130u/l	52	53.1
	>130u/l	46	46.9
	Total	98	100.0

Table 11: frequency of population with increased and normal serum amylase levels

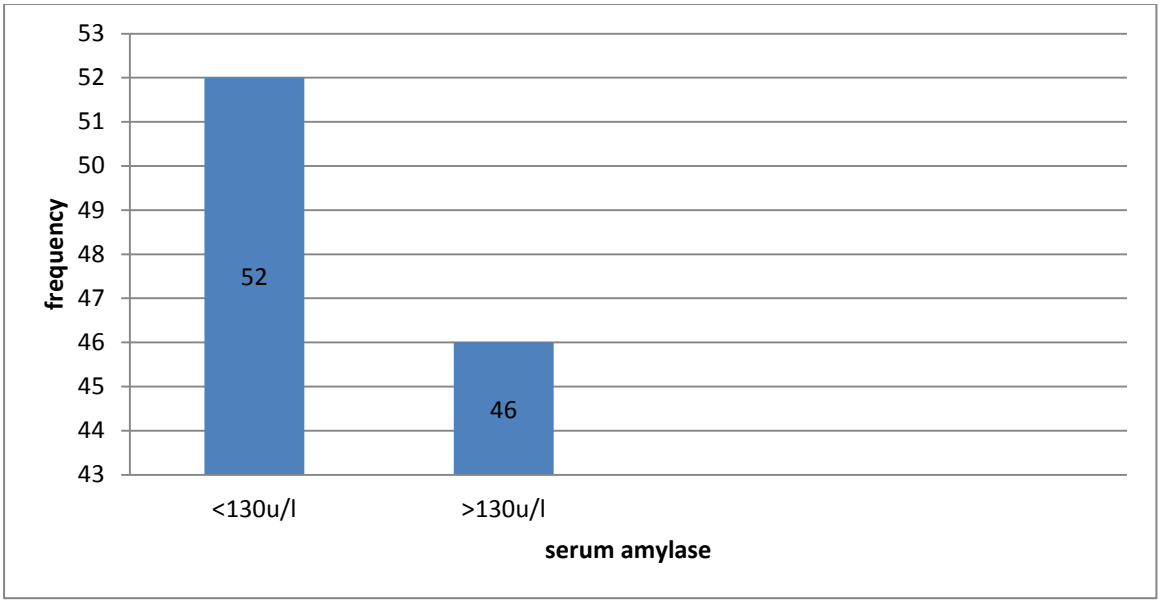

Figure 7: serum amylase distribution

- 52 (53.1%) patients have normal serum amylase levels (<130 u/l)
- 46(46.9%) patients have increased amylase levels (>130u/l)

Serum pseudocholinesterase distribution :

Pseudocholinesterase	Frequency	Percent
<4850 u/l	45	45.9
>4850 u/l	53	54.1
Total	98	100.0

Table 12: serum pseudo cholinesterase levels and its frequency

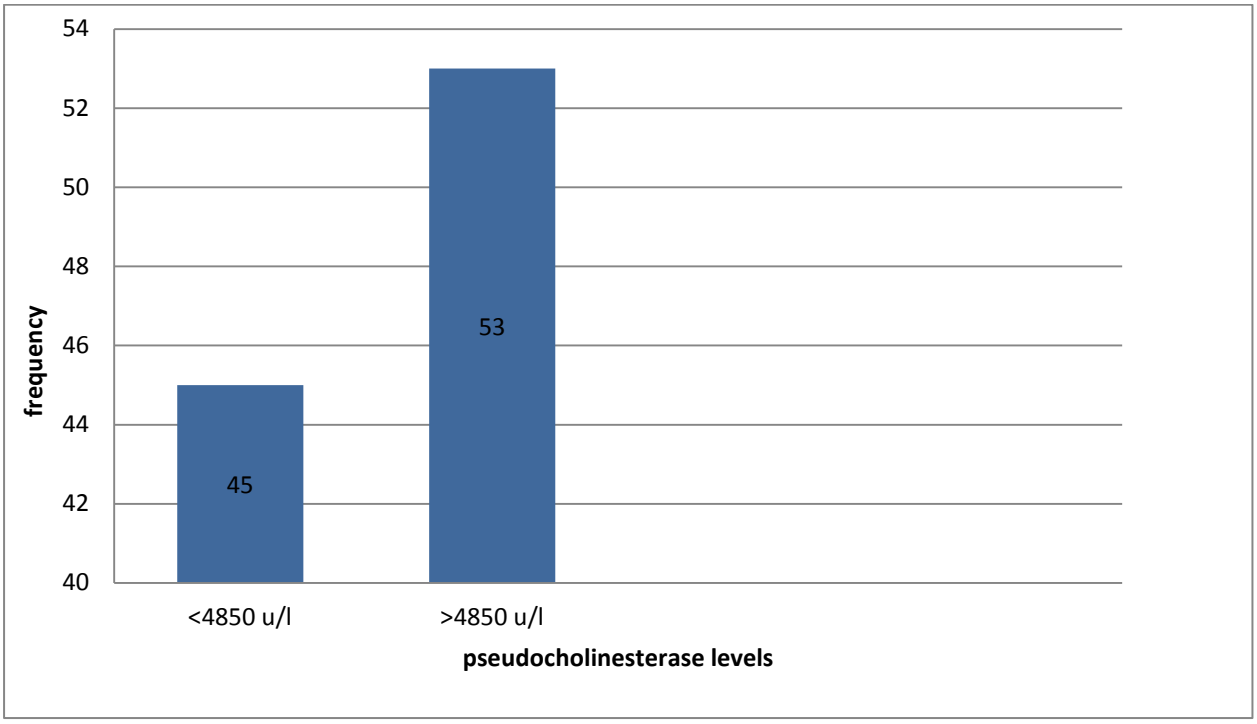

Figure 8 : Estimated pseudo cholinesterase and its frequency

45(45.9%) patients in the study have < 4850 serum pseudo cholinesterase levels

53 (54.1%) patients have >4850 pseudo cholinesterase levels

Peradeniya Organophosphorus Poisoning (POP) Scale severity distribution :

POP Scale	Frequency	Percent
Mild	58	59.2
moderate	20	20.4
severe	20	20.4
Total	98	100.0

Table 13: Frequency of POP scale according to severity

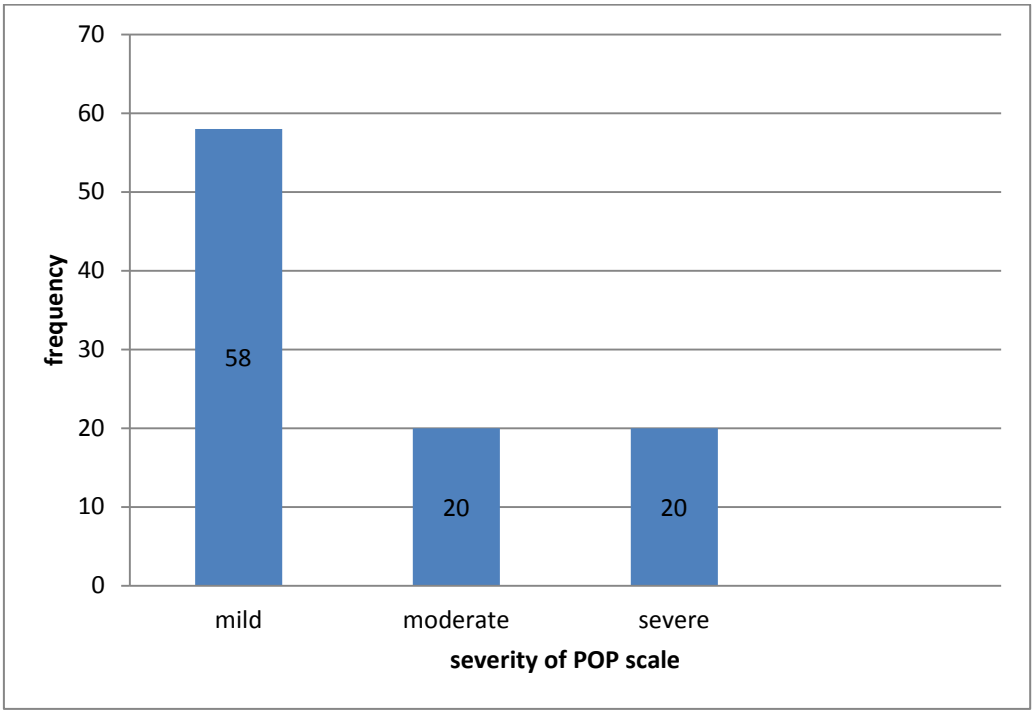

Figure 9: Frequency of POP scale according to severity.

- 58 (59.2%) patients in study had mild severity of poisoning
- 20 (20.4%) patients had moderate severity of poisoning
- 20 (20.4%) patients had severe poisoning

Assessment of ventilator support:

ventilator support required	Frequency	Percent
yes	39	39.8
no	59	60.2
Total	98	100.0

Table 14: Estimation of ventilator support

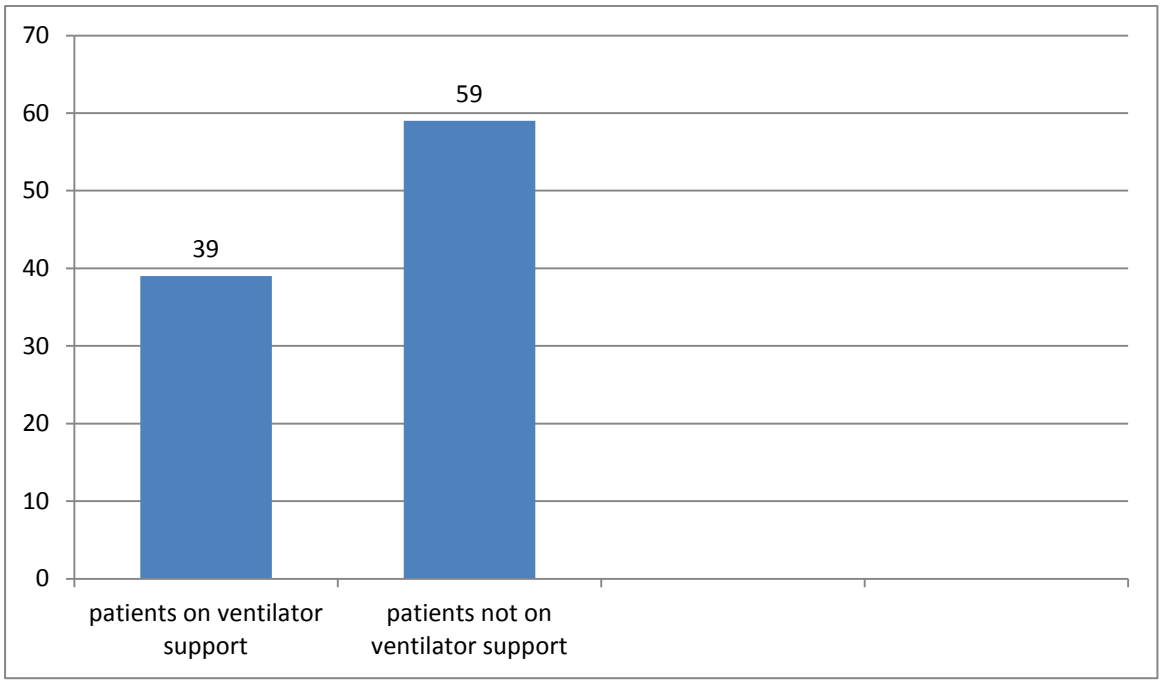

Figure 10: Number of patients who required ventilator support and number of patients who did not require

39 (39.8) patients in the study required ventilator support

59 (69.2) patients did not require ventilator support

Serum Pseudocholinesterase and amylase levels:

		pseudocholinesterase		Total	Chi-square	P-Value
		<4850	>4850			
Amylase	<130u/l	14	38	52		
	>130u/l	31	15	46	16.10	0.001*
	Odds ratio	.400	2.241			

Table 15: correlation between serum amylase and pseudo cholinesterase

Risk estimate for Serum pseudocholinesterase and amylase levels:

	Odds ratio	Confidence interval	
		Lower	upper
Serum amylase	.178	0.75	.425
Cohort Pseudocholinesterase <4850 u/l	.400	.245	.653
Cohort Pseudocholinesterase >4850 u/l	2.241	1.433	.3.504
No of valid cases	98		

Table 16: Odds ratio and confidence interval for serum amylase and pseudo cholinesterase

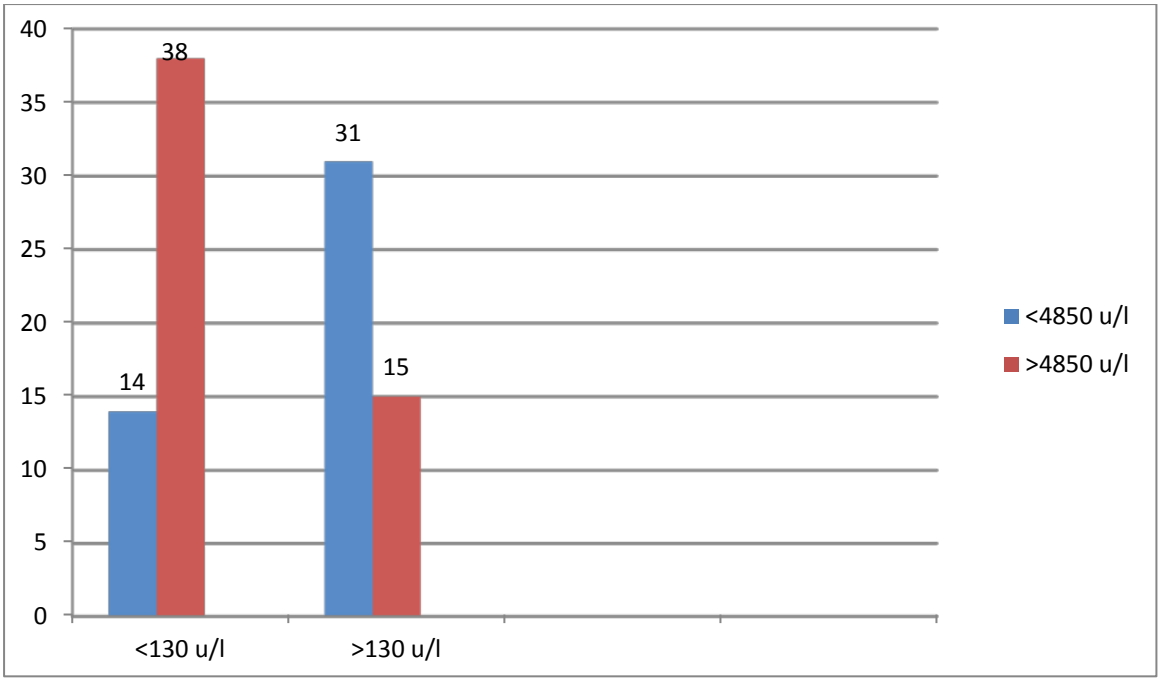

Figure 11:Correlation between serum amylase and pseudocholinesterase

31 patients with increased amylase levels had decreased pseudo cholinesterase levels

There was statistically significant (<0.05) association between serum amylase levels and pseudocholinesterase.

Serum amylase levels and POP scale:

		POP scale			Total	Chi-square	P-Value
		mild	moderate	severe			
Amylase	<130u/l	45	4	3	52		
	>130u/l	13	16	17	46	34.42	0.001*
Total		58	20	20	98		

Table 17: correlation of serum amylase and POP scale

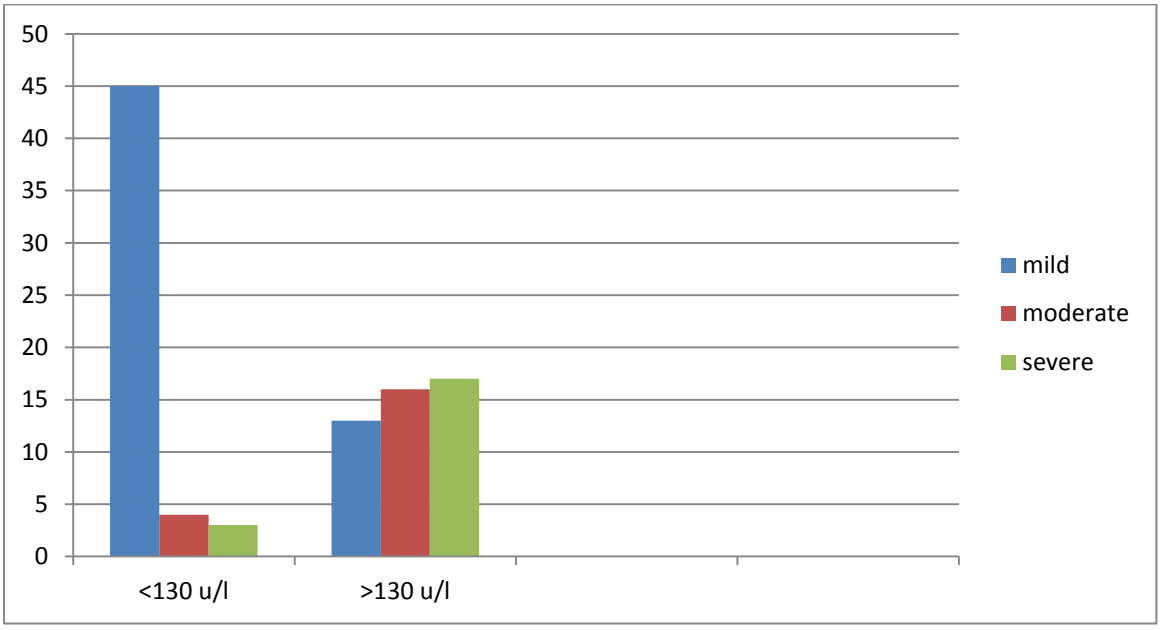

Figure 12 :correlation of serum amylase and POP scale

Patients with increased serum amylase levels (>130u/l) had severe POP score levels , whereas 3 patients with normal serum amylase (<130u/l) had severe POP score.

Serum amylase levels and severity of POP scale shows statistical significance (<0.05)

Serum amylase and ventilator support:

		ventilator support required		Total	Chi-square	P-Value	Odds ratio
Amylase	<130u/l	48	4	52	47.65	0.001*	38.182
	>130u/l	11	35	46			
Total		59	39	98			

Table 18 :serum amylase and need for ventilatory support

Risk Estimate Serum amylase and ventilator support

	Value	95% Confidence Interval	
		Lower	Upper
Odds Ratio for amylase (<130u/l / >130u/l)	38.182	11.222	129.911
For cohort ventilator support required = no	3.860	2.292	6.502
For cohort ventilator support required = yes	.101	.039	.263
N of Valid Cases	98		

Table 19: odds ratio and confidence interval of serum amylase and ventilator support

35 patients with increased serum amylase (>130u/l) required ventilator support compared to 4 patients(<130u/l) with normal amylase levels.

Patients with increased Serum amylase levels and ventilatory support required was statistically significant (<0.05)

Chi square test between amylase and ventilator support shows stastitical significance (<0.05)

DISCUSSION

DISCUSSION

Organophosphate pesticides are common household insecticides used extensively by agricultural communities in the developing countries. Seasonal variations especially in the monsoon season results in financial crisis and drive farmers to suicide by ingestion of agricultural pesticides. Most of these pesticides are sold directly from shops due to lack of special rules and regulations regarding the use and sale of pesticides in countries like India.

Their ease of access and socio-cultural factors play important role in the choice of OP as a self-poison and the incidence is higher in younger, economically active group. In developing countries there is a scarcity of skilled and trained medical professionals in regard to the rational use of antidotes. There is also a scarcity of antidote which may be one of the reasons for higher mortality rates in poisoning management.

Food and Agriculture Organization and WHO recommends that OP compounds belong to toxicity Ia (extremely hazardous) pesticides should not be used in developing countries . But the practice of spraying these “powerful” pesticides continues.

The majority of cases reported in India are due to methylparathion which is widely used by the farmers. It is a highly lipophilic compound where

continuous administration of oximes may be needed for a longer time for its management.

In literature there are many scoring systems based on clinical signs and symptoms to evaluate the intoxication such as APACHE (Acute Physiology and Chronic Health Evaluation) and SAPS (Simplified Acute Physiology Score) to evaluate the clinical severity and to predict the outcome. The Peradeniya Organophosphorus Poisoning (POP) scale assesses the severity of the poisoning based on the symptoms at presentation and is simple to use.Along with clinical assessment, laboratory evaluation also plays a key role in management of OP compound poisoning.

There are various biochemical parameters for diagnosing OP compound poisoning, gold standard is measurement of pseudocholinesterase. Other parameters like serum glucose, CPK, Amylase, lipase have been studied. Studies done by T.n.dubey et al[12], sumathi et al[11], showed an increased prevalence of serum amylase among other biochemical parameters. Excessive cholinergic stimulation of pancreas by OP compound has been thought cause for increase amylase levels.

As there is no much clinical evidence regarding serum amylase levels in assessing severity of OP compound poison , this study was done to assess serum amylase levels in OP compound poisoning as marker of severity and indicator of respiratory failure.

A total of 98 OP compound poisoning patients statisfying the inclusion and exclusion criteria were taken for study. In our study the most common compound used was chlorpyrifos ,phorate and parathion were most common OP compounds used for poisoning.

Mean Age distribution:

Study conducted by Dilip M Rampure et al[6] , Goel et al[9] , Reihman et al[10], kavya S.T et al[15] showed 40 % of patients of patients in 18-30 years of age which was similar to study where 55 (56.1%) patients belong to 18-30 years of age group. The reason for high incidence in this age group 18-30 years could be because of that, this age group was vulnerable to various emotional conflicts that occur during this phase of life , are described to be most stressful, emotionally weak and vulnerable to minor conflicts, failures or disappointments during this phase of life.

Gender distribution:

Studies done by Subhash L.Patil et al [14], Edwin J George et al [16] , Kailas N. Chintale[17] showed male preponderance of 60 % similar to our study , males were 60 (61.2%) and females were 38 (38.8%), but however studies done by Ather et al[21] and Tall et al[22] showed equal male and female ratio of 1:1 . The reason behind males commonly affected was due to as they are main

working group in outdoor field, i.e. they are more involved in spraying crops in the farm and have the whole responsibility of their family.

Socioeconomic factors:

Studies done by Nigam M et al[18], Gupta BD et al[19] , Kailas N. Chintale[17] Muhammad IS et al[20] had higher incidence of poisoning in illiterates than literates similar to our study. Study done by Kora SA. Et al also showed that incidence of pesticide poisoning was more common in married (67%) population than unmarried (33%) which in contrast our study where unmarried were 62% and married were 48%.

Manner of poisoning :

Studies done by Dayanand et al[23], Subhash et al[14], Gupta et al[19] showed suicidal was the most common manner of poisoning which was similar to our study the most common manner for poisoning was suicidal-90 (91.8%) followed by accidental – 6(6.12%) and homicidal- 2(2.04%).

Type of OP Compound consumed :

Chlorpyrifos was most common compound consumed in study done by Edwin et al[16] which is similar to our study chlorpyrifos (40%) and followed by parathion(32%) whereas Methyl parathion was also the most common

poison detected in the studies of Indranil et al[24] Shivakumar S[25] and T. Selvaraj et al[26] . Mortality rate was higher in patients consuming parathion compound poisoning compared to chlorpyrifos and other compounds.

Clinical presentation:

Studies done by T. Selvaraj et al[26] Edwin et al[16] and Dayanand et al[23] showed Nausea and vomiting was the most common clinical feature , followed by Excessive secretions and muscular weakness which was similar to our study where nausea was seen in 80 (81%) of patients, followed by vomiting in 64 (65%), diarrhoea in 42(42.8%) ,breathlessness in 38 (38.7%) but studies done by Goswamy R et al[27] showed breathlessness (72%) as a common clinical feature.This can be due to excessive muscarinic receptor stimulation or by gastrointestinal irritation of op compounds.

Random blood sugar and OP compounds :

Hyperglycemia was noted in 70 (71%) of op compound poisoning[30] which was similar to the study done by meler d et al[28] and shobha et al[29] which was noted in 82% of patients and it was thought to be due to oxidative stress, stimulation of adrenals, release of cathecholamines ,renal tubular damage and also hyperamylasemia causing pancreatitis can result in hyperglycemia .

Serum Amylase levels :

In our study , 46(46.9%) patients have increased amylase levels (>130u/l), which was similar to the study done by lee wc et al[31] and Singh s et al reported hyperamylasemia to be present in 36% and 46.95% of the OP compound poisoning patients respectively[7].This was due to excessive cholinergic stimulation of pancreas causing increased serum amylase levels.

POP score:

In our study 58 (59.2%) patients in study had mild grade, 20 (20.4%) patients had moderate grade and 20 (20.4%) patients had severe grade .These findings were similar to the study done by Subhash L.Patil et al[14] where 70% of patients had mild grade and 3.3% severe grade.

Serum amylase and pseudocholinesterase levels:

In our study statistically significant association was present between amylase levels and pseudocholinesterase levels, similar to the study conducted by Sharan Badiger et al[8] showed 68 % of patients with hyperamylasemia had decrease in pseudocholinesterase levels.

Serum amylase and pop score:

In our study , statistically significant association is present between serum amylase and pop score , more number of patients with hyperamylasemia have severe pop score.17 patients with increased serum amylase levels (>130u/l) had severe pop score levels , whereas only 3 patients with normal serum amylase (<130u/l) had severe pop score. These findings are similar to the study done by similar to the studies done by K.Bhattacharya et al[13] and dubey et al[12].

Serum amylase and ventilator support:

Increased serum amylase levels was found in patients who developed respiratory failure and predicted the need for ventilator support. Studies done by sumathi et al[11] also reported that the elevation of amylase levels was predictive of subsequent respiratory failure and requirement of mechanical ventilation.

CONCLUSION

CONCLUSION

- Hyperamylasemia is common in OP poisoning, due to excessive cholinergic stimulation of pancreas.
- Amylase estimation can be used as a prognostic indicator along with the serum cholinesterase activity.
- Estimation of Serum amylase levels in OP compound poisoning will help in assessing severity of poisoning, and also need for ventilator support.
- In our study, out of 98 patients studied, serum amylase was significantly elevated in 46 patients (46.9%).
- It enables the early recognition of severity and also helps to identify those at risk of developing the complications of Organophosphorus poisoning.
- It also helped in identifying patients at risk of developing respiratory failure.
- There was an inversely proportional relationship between serum amylase and pseudo cholinesterase levels i.e. increase in serum amylase levels there was decrease in pseudo cholinesterase levels.
- Increase in Serum amylase indicates the severity of poisoning predicted by pop score, majority of patients with severe pop score had an increased amylase levels. The present study analyzed, that there was statistically significant association present between serum amylase, pop score, pseudocholinestearse levels and ventilator support.

SUMMARY

SUMMARY

It was a hospital based cross sectional study conducted in a tertiary health hospital. Sample size was 98.

The objectives of the study were to estimate serum amylase levels in Organophosphorus compound poisoning and to correlate serum amylase levels with severity of OP compound poisoning by using Peradeniya Organophosphorus Poisoning (POP) scale and to assess serum amylase levels in Organophosphorus compound poisoning as a need for ventilatory support.

A majority of patients belonged to age group of 18-31 years, most of them were male.46.9% of patients had increased amylase levels out of 98 patients studied.

Our Study showed a statistically significant relationship between serum amylase levels, Pseudocholinesterase levels, pop scale and ventilator support.

This study signifies the importance of serum amylase levels estimation in OP compound poisoning patients in predicting the severity and need for ventilator support.

BIBLIOGRAPHY

REFERENCES

1. Sundaray K, Ratheesh KJ. Organophosphorous poisoning: Current Management guidelines. API update 2010;420-6.
2. Jesslin J, Adepu R, Churi S. Assessment of prevalence and mortality incidences due to poisoning in a South Indian tertiary care teaching hospital. Indian J Pharm Sci. 2010;72:587-91.

3 Amanvermez R, Baydın A, Yardan T, Başol N, Günay M. Emergency laboratory abnormalities in suicidal patients with acute organophosphate poisoning. Turkish J Biochem 2010;35:29‑34.

4 Thundiyil JG, Stober J, Besbelli N, Pronczuk J. Acute pesticide poisoning: A proposed classification tool. Bull World Health Organisation 2008;86:2059.

5 Jesslin J, Adepu R, Churi S. Assessment of prevalence and mortality incidences due to poisoning in a South Indian tertiary care teaching hospital. Indian J Pharm Sci 2010;72:58791.

6 Dilip M Rampure , I. B. Ganiger , CH. Ellareddy A Study on Serum Amylase Levels in Acute Organophoshorous Poisoning and It's Relationship with Clinical Severity And Outcome Global J Research Analysis 2015;77-9850

7 Singh S, Bhardwaj U, Verma SK, Bhalla A, Gill K. Hyperamylasemia and acute pancreatitis following anticholinesterase poisoning. Hum Exp Toxicol 2007;26:67-71

8 Sharan Badiger , Vishok M. Study of Serum Amylase and Serum Cholinesterase in Organophosphorus Poisoning J Krishna Inst of Med Sci Univ 2016;28-87-91.

9 Goel A, Joseph S, Dutta TK. Organophosphate poisoning: Predicting the need for ventilator support. Journal of association of physicians of India 1998;46:786-90

10 Rehiman S, Lohani SP, Bhattarai MD. Correlation of serum cholinesterase level, clinical score at presentation and severity of organophosphorus poisoning. J Nepal Med Assoc 2008;47(170):47-52.

11 Sumathi ME, Kumar SH, Shashidhar KN,Takkalaki N. Prognostic significance of various biochemical parameters in acute organophosphorus poisoning. Toxicol Int 2014;21:167-71.

12 T. N. Dubey , Sudhanshu Yadav , K K. Kawre. Correlation of Severity of Organophoshorus Poisoning as Assessed by Peradeniya Organophosphorus Poisoning Scale with Serum Amylase and CPK Level Int J of Contemporary Medi Res 2016;2454-7379

13 Bhattacharyya K, Phaujdar S, Sarkar R et al, Serum creatine phosphokinase: a probable marker of severity in organophosphorus poisoning. Toxicol.Interna. 2011;18: 117-123

14 Dr.Subhash L.Patil, Dr. Praveen Vasepalli .Prognostic value of clinical and lab parameters in assessing the severity of organophosphorous compound poisoning Indian J of Basic and Applied Med Res; December 2014;77- 91.

15 Kavya ST, Srinivas V, Chandana, Madhumati R. Clinical Profile of patients with Organophosphorus Poisoning in an Intensive Care Unit in a tertiary hospital. International Journal of Clinical Cases and Investigations 2012 Oct;4(2):24-31.

16 K Edwin J George, Jayaraj K, John J Manjaly , Raghunath M .Clinical profile and outcome of organophosphate poisoning cases in a ter care hospital in central kerala. International J of Recent Trends in Sci And Tech 2015 ; 338-343.

17 Kailas N. Chintale , Sanjay V. Patne, Sanjay S. Chavan. Clinical profile of organophosphorus poisoning patients at rural tertiary health care centre International Journal of Advances in Medicine 2016 ;3(2):268-274.

18 Nigam M, Jain AK, Dubey BP, Sharma VK. Trends of Organophosphorus Poisoning in Bhopal region an autopsy based

study. Journal of Indian Academy of Forensic Medicine. 2004;26(2):61-5.

19 Gupta BD, Vaghela PC. Profile of Fatal Poisoning in and around Jamnagar. Journal of Indian Academy of Forensic Medicine 2005;27(3):145-8. 12.

20 Muhammad IS, Rushd J, Rai M. The analysis of organophosphates poisoning cases treated at Bahawal Victoria Hospital, Bahawalpur in 2000- 2003. Pakistan Journal of Medical Sciences. 2006; 22(3):244-9.

21 Ather NA, Ara J, Khan EA, Sattar RA, Durrani R. Acute organophosphate insecticide poisoning. J Surg Pak. 2008;13:71–4.

22 Tall A, Ly AB, Nabeth P, Sall AA, Sarr FD, Faye J, et al.Epidemiological investigation of death cases by pesticide poisoning. J Agric Biotechnol Sustainable Develop. 2010;2:51–5.

23 Dayanand Raddi, Anikethana G V. Clinical profile of organophosphorus poisoning in a tertiary care hospital. Indian Journal of Basic and Applied Medical Research; December 2014:4(1);P 14-22.

24 Indranil Banerjee, SK Tripathi, and A Sinha Roy1 N Am J Med Sci. 2012 Mar;4(3):147–150.

25 Shivakumar S, Mohammed Ishaq R, Raghavan K, Geetha S. Organophosphorus poisoning –a study of 165 cases from chennai, india. .

26 T. Selvaraj , T. Sudharson. Demographic and Clinical Profile of Organophosphorus Poisoning cases in a Medical College Hospital, Tamil Nadu .Indian Journal of Forensic and Community Medicine, June 2016;3(2):124-127.

27 Goswamy R., Chaudary A., Mahashur A. A study of respiratory failure in organophosphate and carbamate poisoning. Heart Lung 1994;23(6):466-72.

28 Meller D, Fraser I, Kryger M. Hyperglycemia in anticholinesterase poisoning. Can Med Assoc J 1981;124:745-8.

29 Shobha TR, Prakash O. Glycosuria in organophosphate and carbamate poisoning J Assoc Physicians India 2000;48:1197-9.

30 Weizman Z, Sofer S. Acute pancreatitis in children with anticholinesterase insecticide intoxication. Pediatrics 1992;90:204-6.

31 Lee WC, Yang CC, Deng JF, Wu ML, JiinGer, Lin HC, Chang FY and Lee SD. The Clinical Significance of Hyperamylasemia in Organophosphate Poisoning. J Toxicol Clin Toxicol 1998;36(7):673-81.

32 Senarathna L, Jayamanna SF, Kelly PJ, Buckley NA, Dibley MJ, Dawson AH. Changing epidemiologic patterns of deliberate self poisoning in a rural district of Sri Lanka. BMC Public Health. 2012;12:593

33 Balme KH, Roberts JC, Glasstone M, Curling L, Rother HA, London L, et al. Pesticide poisonings at a tertiary children's hospital in South Africa: An increasing problem. Clin Toxicol (Phila) 2010;48:928–34.

34 Peter JV, Jerobin J, Nair A, Bennett A, Samuel P, Chrispal A, et al. Clinical profile and outcome of patients hospitalized with dimethyl and diethyl organophosphate poisoning. Clin Toxicol (Phila) 2010;48:916–23.

35 Peter JV, Cherian AM. Organic insecticides. Anaesth Intensive Care. 2000;28:11–21.

36 Wadia RS, Sadagopan C, Amin RB, Sardesai HV. Neurological manifestations of organophosphorous insecticide poisoning. J Neurol Neurosurg Psychiatry. 1974;37:841–7. Namba T. Cholinesterase inhibition by organophosphorus compounds and its clinical effects. Bull World Health Organ. 1971;44:289–307.

37 Robenshtok E, Luria S, Tashma Z, Hourvitz A. Adverse reaction to atropine and the treatment of organophosphate intoxication. Isr Med Assoc J. 2002;4:535–9.

38 Singh G, Khurana D. Neurology of acute organophosphate poisoning. Neurol India. 2009;57:119–25

39 Singh S, Sharma N. Neurological syndromes following organophosphate poisoning. Neurol India. 2000;48:308–13.

40 Eddleston M, Mohamed F, Davies JO, Eyer P, Worek F, Sheriff MH, et al. Respiratory failure in acute organophosphorus pesticide self-poisoning. QJM. 2006;99:513–22

41 Noshad H, Ansarin K, Ardalan MR, Ghaffari AR, Safa J, Nezami N. Respiratory failure in organophosphate insecticide poisoning. Saudi Med J. 2007;28:405–7.

42 12. Anand S, Singh S, Nahar Saikia U, Bhalla A, Paul Sharma Y, Singh D. Cardiac abnormalities in acute organophosphate poisoning. Clin Toxicol (Phila) 2009;47:230–5.

43 Karki P, Ansari JA, Bhandary S, Koirala S. Cardiac and electrocardiographical manifestations of acute organophosphate poisoning. Singapore Med J. 2004;45:385–9.

44 Saadeh AM, Farsakh NA, al-Ali MK. Cardiac manifestations of acute carbamate and organophosphate poisoning. Heart. 1997;77:461–4.

45 Lee P, Tai DY. Clinical features of patients with acute organophosphate poisoning requiring intensive care. Intensive Care Med. 2001;27:694–9.

46 Brahmi N, Mokline A, Kouraichi N, Ghorbel H, Blel Y, Thabet H, et al. Prognostic value of human erythrocyte acetyl cholinesterase in acute organophosphate poisoning. Am J Emerg Med. 2006;24:822–7.

47 Bobba R, Venkataraman BV, Pais P, Joseph T. Correlation between the severity of symptoms in organophosphorus poisoning and

cholinesterase activity (RBC and plasma) in humans. Indian J Physiol Pharmacol. 1996;40:249–52.

48 Eddleston M, Eyer P, Worek F, Sheriff MH, Buckley NA. Predicting outcome using butyrylcholinesterase activity in organophosphorus pesticide self-poisoning. QJM. 2008;101:467–74

49 Atri A, Chang MS, Strichartz GR. Cholinergic pharmacology. In: Golan DE, Tashjian AH, Armstrong EJ, Armstrong AW, editors. Principles of Pharmacology: The Pathophysiologic Basis of Drug Therapy. 3rd ed. Philadelphia, PA: Lippincott Williams and Wilkins; 2011. pp. 110–31.

50 Kalamida D, Poulas K, Avramopoulou V, Fostieri E, Lagoumintzis G, Lazaridis K, et al. Muscle and neuronal nicotinic acetylcholine receptors. Structure, function and pathogenicity. FEBS J. 2007;274:3799–845.

51 Sellin AK, Shad M, Tamminga C. Muscarinic agonists for the treatment of cognition in schizophrenia. CNS Spectr. 2008;13:985–96.

52 Abrams P, Andersson KE, Buccafusco JJ, Chapple C, de Groat WC, Fryer AD, et al. Muscarinic receptors: Their distribution and function in body systems, and the implications for treating overactive bladder. Br J Pharmacol. 2006;148:565–78.

53 Jayawardane P, Senanayake N, Buckley NA, Dawson AH. Electrophysiological correlates of respiratory failure in acute organophosphate poisoning: Evidence for differential roles of muscarinic and nicotinic stimulation. Clin Toxicol (Phila) 2012;50:250–3.

54 Jayawardane P, Senanayake N, Dawson A. Electrophysiological correlates of intermediate syndrome following acute organophosphate poisoning. Clin Toxicol (Phila) 2009;47:193–205.

55 McDonough JH, Jr, Clark TR, Slone TW, Jr, Zoeffel D, Brown K, Kim S, et al. Neural lesions in the rat and their relationship to EEG delta activity following seizures induced by the nerve agent soman. Neurotoxicology. 1998;19:381–91

56 Rickett DL, Glenn JF, Beers ET. Central respiratory effects versus neuromuscular actions of nerve agents. Neurotoxicology. 1986;7:225–36.

57 Chang FC, Foster RE, Beers ET, Rickett DL, Filbert MG. Neurophysiological concomitants of soman-induced respiratory depression in awake, behaving guinea pigs. Toxicol Appl Pharmacol. 1990;102:233–50.

58 Dickson EW, Bird SB, Gaspari RJ, Boyer EW, Ferris CF. Diazepam inhibits organophosphate-induced central respiratory depression. Acad Emerg Med. 2003;10:1303–6.

59 Bardin PG, Van Eeden SF. Organophosphate poisoning: Grading the severity and comparing treatment between atropine and glycopyrrolate. Crit Care Med. 1990;18:956–60.

60 Kventsel I, Berkovitch M, Reiss A, Bulkowstein M, Kozer E. Scopolamine treatment for severe extra-pyramidal signs following organophosphate (chlorpyrifos) ingestion. Clin Toxicol (Phila) 2005;43:877–9.

61 Weissman BA, Raveh L. Therapy against organophosphate poisoning: The importance of anticholinergic drugs with antiglutamatergic properties. Toxicol Appl Pharmacol. 2008;232:351–8.

62 Weissman BA, Raveh L. Multifunctional drugs as novel antidotes for organophosphates poisoning. Toxicology. 2011;290:149–55.

63 Sener EB, Ustun E, Kocamanoglu S, Tur A. Prolonged apnea following succinylcholine administration in undiagnosed acute organophosphate poisoning. Acta Anaesthesiol Scand. 2002;46:1046–8.

64 Pérez Guillermo F, Martinez Pretel CM, Tarín Royo F, Peña Macias MJ, Alvarez Ossorio R, Alvarez Gómez JA, et al. Prolonged suxamethonium-induced neuromuscular blockade associated with organophosphate poisoning. Br J Anaesth. 1988;61:233–6.

65 Jaksa RJ, Palahniuk RJ. Attempted organophosphate suicide: A unique cause of prolonged paralysis during electroconvulsive therapy. Anesth Analg. 1995;80:832–3.

66 Weeks DB, Ford D. Prolonged suxamethonium-induced neuromuscular block associated with organophosphate poisoning. Br J Anaesth. 1989;62:237. Peter JV, Moran JL, Graham PL. Advances in the management of organophosphate poisoning. Expert Opin Pharmacother. 2007;8:1451–64.

67 Buckley NA, Eddleston M, Li Y, Bevan M, Robertson J. Oximes for acute organophosphate pesticide poisoning. Cochrane Database Syst Rev. 2011:CD005085.

68 Eddleston M, Buckley NA, Eyer P, Dawson AH. Management of acute organophosphorus pesticide poisoning. Lancet. 2008;371:597–607.

69 Marrs TC. Organophosphate poisoning. Pharmacol Ther. 1993;58:51–66.

70 Rusyniak DE, Nañagas KA. Organophosphate poisoning. Semin Neurol. 2004;24:197–204

71 Faiz MS, Mughal S, Memon AQ. Acute and late complications of organophosphate poisoning. J Coll Physicians Surg Pak. 2011;21:288–90.

72 Karalliedde L, Baker D, Marrs TC. Organophosphate-induced intermediate syndrome: Aetiology and relationships with myopathy. Toxicol Rev. 2006;25:1–14.

73 Peter JV, Prabhakar AT, Pichamuthu K. Delayed-onset encephalopathy and coma in acute organophosphate poisoning in humans. Neurotoxicology. 2008;29:335–42.

74 Brahmi N, Gueye PN, Thabet H, Kouraichi N, Ben Salah N, Amamou M. Extrapyramidal syndrome as a delayed and reversible complication of acute dichlorvos organophosphate poisoning. Vet Hum Toxicol. 2004;46:187–9.

75 Jokanovic M, Stukalov PV, Kosanovic M. Organophosphate induced delayed polyneuropathy. Curr Drug Targets CNS Neurol Disord. 2002;1:593–602.

76 Okudera H. Clinical features on nerve gas terrorism in Matsumoto. J Clin Neurosci. 2002;9:17–21.

77 Yanagisawa N, Morita H, Nakajima T. Sarin experiences in Japan: Acute toxicity and long-term effects. J Neurol Sci. 2006;249:76–85.

78 Meggs WJ. Permanent paralysis at sites of dermal exposure to chlorpyrifos. J Toxicol Clin Toxicol. 2003;41:883–6.

79 Peiris JB, Fernando R, De Abrew K. Respiratory failure from severe organophosphate toxicity due to absorption through the skin. Forensic Sci Int. 1988;36:251–3.

80 Yardan T, Baydin A, Aygun D, Karatas AD, Deniz T, Doganay Z. Late-onset intermediate syndrome due to organophosphate poisoning. Clin Toxicol (Phila) 2007;45:733–4.

ANNEXURE

PROFORMA

Sl. No: **Date:**

OP/ IP No:

Name:

Age:

Occupation:

Address:

CHIEF COMPLAINTS:

HISTORY OF PRESENTING ILLNESS:

PAST MEDICAL HISTORY:

FAMILY HISTORY :

PERSONAL HISTORY :

DRUG HISTORY :

GENERAL PHYSICAL EXAMINATION:

VITAL DATA :

SYSTEMIC EXAMINATION:

- CARDIOVASCULAR SYSTEM:

- RESPIRATORY SYSTEM:

- GASTROINTESTINAL SYSTEM:

- CENTRAL NERVOUS SYSTEM :

INVESTIGATIONS:

1. CBC:

2. RFT:

3. Urine routine:

4. Random blood sugar:

5. serum amylase:

6. Serum lipase:

7. Serum pseudocholinesterase:

8. Lipid profile:

9. Serum electrolytes:

PROVISIONAL DIAGNOSIS:

INFORMED CONSENT FORM

Study on the hyperamylasemia as an indicator of severity and predictor of respiratory failure in organophosphorous compound poisoning

STUDY NUMBER:

SUBJECT'S NAME: **HOSPITAL NUMBER:**

AGE:

Study on the hyperamylasemia as an indicator of severity and predictor of respiratory failure in organophosphorous compound poisoning will bring to limelight the importance and potentiate the clinical application of serum amylase as an predictor of severity and respiratory failure

If you agree to participate in the study we will collect information (as per Performa) from you or a person responsible for you or both. We will collect the treatment and relevant details from your hospital record. This information collected will be used for only dissertation and publication. This study has been reviewed by the institutional ethical committee. The care you will get will not change if you don't wish to participate. You are required to sign/ provide thumb impression only if you voluntarily agree to participate in this study.

I understand that I remain free to withdraw from the study at any time and this will not change my future care. I have read or have been read to me and understood the purpose of the study, the procedure that will be used, the risk and benefits associated with my involvement in the study and the nature of information that will be collected and disclosed during the study. I have had the opportunity to ask my questions regarding various aspects of the study and my questions are answered to my satisfaction. I, the undersigned agree to participate in this study and authorize the collection and disclosure of my personal information for dissertation.

Subject name

(Parents / Guardians name)

DATE: SIGNATURE /THUMB IMPRESSION

ಮಾಹಿತಿಯುಕ್ತ ಸಮ್ಮತಿಯ ನಮೂನೆ

ಆರ್ಗಾನೋಫಾಸ್ಫೋರಸ್ ಸಂಯುಕ್ತ ವಿಷ ಒಂದು ಕಠೋರತೆಯ ಸೂಚಕ ಮತ್ತು ಉಸಿರಾಟದ ವೈಫಲ್ಯದ ಊಹಿಸುವಲ್ಲಿ ಹೈಪರಾಮೈಲಾಸ್ಸೆಮಿಯಾ ಅಧ್ಯಯನ

ಅಧ್ಯಯನ ಸಂಖ್ಯೆ:

ಪ್ರಯೋಗಾರ್ಥಿಯ ಹೆಸರು: ಆಸ್ಪತ್ರೆಯ ಸಂಖ್ಯೆ:

ಏಜ್:

ತೀವ್ರತೆ ಮತ್ತು ಆರ್ಗಾನೋಫಾಸ್ಫೋರಸ್ ಸಂಯುಕ್ತ ವಿಷ ಉಸಿರಾಟದ ವೈಫಲ್ಯದ ಊಹಿಸುವ ಒಂದು ಸೂಚಕವಾಗಿ ಹೈಪರಾಮೈಲಾಸ್ಸೆಮಿಯಾ ಸ್ಟಡಿ ಆನ್ ಪ್ರಾಮುಖ್ಯತೆಯನ್ನು ಪ್ರಚಾರದಿಂದ ತನ್ನಿ ಮತ್ತು ತೀವ್ರತೆ ಮತ್ತು ಉಸಿರಾಟದ ತೊಂದರೆಯಿಂದ ಒಂದು ಊಹಿಸುವಲ್ಲಿ ಸೀರಮ್ ಎಮಿಲೇಸ್ ವೈದ್ಯಕೀಯ ಅಪ್ಲಿಕೇಶನ್ ಸಾಮರ್ಥ್ಯವನ್ನು ಮಾಡುತ್ತದೆನೀವು ಅಧ್ಯಯನದಲ್ಲಿ ಭಾಗವಹಿಸಲು ಒಪ್ಪಿದಲ್ಲಿ ನಾವು ನೀವು ಅಥವಾ ನೀವು ಅಥವಾ ಎರಡೂ ನಿರ್ವಹಿಸುವ ವ್ಯಕ್ತಿ ರಿಂದ (ಪರ್ಫಾ ಪ್ರಕಾರ) ಮಾಹಿತಿ ಸಂಗ್ರಹಿಸುತ್ತದೆ. ನಾವು ನಿಮ್ಮ ಆಸ್ಪತ್ರೆಯ ದಾಖಲೆ ಚಿಕಿತ್ಸೆ ಮತ್ತು ಸಂಬಂಧಿಸಿದ ವಿವರಗಳನ್ನು ಸಂಗ್ರಹಿಸುತ್ತದೆ. ಸಂಗ್ರಹಿಸಿದ ಈ ಮಾಹಿತಿಯನ್ನು ಪ್ರೌಢಪ್ರಬಂಧದಲ್ಲಿ ಮತ್ತು ಪ್ರಕಟಣೆಗೆ ಬಳಸಲಾಗುತ್ತದೆ. ಈ ಅಧ್ಯಯನವು ಸಾಂಸ್ಥಿಕ ನೈತಿಕ ಸಮಿತಿಯು ವಿಮರ್ಶಿಸುತ್ತದೆ ಮಾಡಲಾಗಿದೆ. ನೀವು ಭಾಗವಹಿಸಲು ಇಚ್ಛಿಸದಿದ್ದರೆ ನೀವು ಪಡೆಯುತ್ತಾನೆ ರಕ್ಷಣೆ ಬದಲಾಗುವುದಿಲ್ಲ. ನೀವು / ಸೈನ್ ನೀವು ಸ್ವಯಂಪ್ರೇರಣೆಯಿಂದ ಈ ಅಧ್ಯಯನದಲ್ಲಿ ಭಾಗವಹಿಸಲು ಒಪ್ಪುತ್ತೀರಿ ಮಾತ್ರ ಹೆಬ್ಬೆಟ್ಟಿನ ಗುರುತು ಒದಗಿಸುವ ಅಗತ್ಯವಿದೆ.ನಾನು ಯಾವುದೇ ಸಮಯದಲ್ಲಿ ಅಧ್ಯಯನ ಹಿಂದಕ್ಕೆ ಉಚಿತ ಉಳಿದು ಈ ನನ್ನ ಭವಿಷ್ಯದ ಕಾಳಜಿ ಬದಲಾಗುವುದಿಲ್ಲ ಎಂದು ಅರ್ಥ. ನಾನು ಓದಲು ಅಥವಾ, ಅಪಾಯ ಮತ್ತು ನನ್ನ ಅಧ್ಯಯನದಲ್ಲಿ ತೊಡಗಿರುವ ಮತ್ತು ಸಂಗ್ರಹಿಸಿ ಅಧ್ಯಯನ ಮಾಡುವ ಸಂದರ್ಭದಲ್ಲಿ ಬಹಿರಂಗ ಎಂದು ಮಾಹಿತಿ ಸ್ವರೂಪ ಸವಲತ್ತುಗಳು ಬಳಸಲಾಗುತ್ತದೆ ಎಂದು ವಿಧಾನ ನನಗೆ ಓದಲು ಮತ್ತು ಅಧ್ಯಯನದ ಉದ್ದೇಶ ಗ್ರಹಿಸಲಾಗಿದೆ. ನಾನು ಅಧ್ಯಯನ ವಿವಿಧ ಅಂಶಗಳನ್ನು ಬಗ್ಗೆ ನನ್ನ ಪ್ರಶ್ನೆಗಳನ್ನು ಕೇಳಲು ಅವಕಾಶ ಹೊಂದಿದ್ದರು ಮತ್ತು ನನ್ನ ಪ್ರಶ್ನೆಗಳಿಗೆ ನನ್ನ ತೃಪ್ತಿ ಉತ್ತರಿಸುತ್ತದೆ. ನಾನು ರುಜುಮಾಡಿರುವ ಈ ಅಧ್ಯಯನದಲ್ಲಿ ಭಾಗವಹಿಸಲು ಮತ್ತು ಪ್ರೌಢಪ್ರಬಂಧದಲ್ಲಿ ನನ್ನ ವೈಯಕ್ತಿಕ ಮಾಹಿತಿಯ ಸಂಗ್ರಹಣೆ ಮತ್ತು ಬಹಿರಂಗಪಡಿಸುವಿಕೆಯ ಅಧಿಕೃತಗೊಳಿಸಲು ಒಪ್ಪುತ್ತೇನೆ.

ವಿಷಯ ಹೆಸರು

(ಪಾಲಕರು / ಗಾರ್ಡಿಯನ್ಸ್ ಹೆಸರು) ಅರ್ಜಿದಾರರ ಸಹಿ / ಹೆಬ್ಬೆಟ್ಟಿನ

ಗುರುತು ದಿನಾಂಕ:

MASTER CHART

MASTER CHART

sl.no	name	age	sex	hospital number	amylase	Pseudoch-olinesterase	pop scale	ventilator support required
1	amyed	35	male	262857	<130 u/l	>4850 u/l	mild	no
2	venkateshappa	30	male	263313	<130u/l	>4850 u/l	mild	no
3	srinivas	20	male	265188	<130u/l	>4850 u/l	mild	no
4	ravanappa	40	male	255967	>130u/l	<4850 u/l	mild	no
5	prathap	25	male	267367	<130u/l	>4850 u/l	mild	no
6	thilak kumar	18	male	268150	<130u/l	<4850 u/l	severe	yes
7	subramani	25	male	268685	>130u/l	<4850 u/l	moderate	yes
8	manasa	23	female	263988	<130u/l	>4850 u/l	mild	no
9	aruna	20	female	266974	>130u/l	<4850 u/l	mild	no
10	savithramma	20	female	268260	>130u/l	<4850 u/l	severe	yes
11	vasantha	62	female	270598	>130u/l	<4850 u/l	moderate	yes
12	manju	21	female	270974	>130u/l	>4850 u/l	severe	yes
13	radhamma	30	female	277387	>130u/l	<4850 u/l	moderate	yes
14	roopa	40	female	280910	>130u/l	<4850 u/l	mild	no
15	lakshmi	32	female	282374	>130u/l	>4850 u/l	moderate	yes
16	samsheda	25	female	286075	>130u/l	<4850 u/l	severe	yes
17	monika	18	female	287529	>130u/l	<4850 u/l	moderate	yes
18	ram prasad	32	male	268707	<130u/l	>4850 u/l	mild	no
19	prathap	25	male	270241	<130u/l	>4850 u/l	mild	no
20	harshitha	20	female	278150	>130u/l	>4850 u/l	moderate	yes
21	lakshmi	23	female	282374	>130u/l	>4850 u/l	severe	yes
22	sanjana	35	female	293357	>130u/l	<4850 u/l	mild	no

23	ravi	32	male	269428	>130u/l	<4850 u/l	moderate	yes
24	venkatareddy	65	male	272739	<130u/l	>4850 u/l	severe	no
25	nagesh	26	male	273136	<130u/l	>4850 u/l	mild	no
26	parvathamma	35	female	296909	>130u/l	<4850 u/l	moderate	yes
27	janaki	20	female	309752	>130u/l	<4850 u/l	severe	yes
28	suma	20	female	318691	>130u/l	<4850 u/l	moderate	yes
29	tresh raj	60	male	386630	>130u/l	<4850 u/l	moderate	yes
30	suresh	22	male	395722	< 130u/l	>4850 u/l	severe	no
31	sampath kumar	28	male	397180	<130u/l	>4850 u/l	moderate	yes
32	ravi	32	male	269428	>130u/l	<4850 u/l	moderate	yes
33	venkatareddy	65	male	272739	<130u/l	>4850 u/l	mild	no
34	nagesh	26	male	273136	<130u/l	>4850 u/l	mild	no
35	jharje	60	male	275174	>130u/l	>4850 u/l	severe	no
36	naresh	19	male	277280	<130u/l	>4850 u/l	mild	no
37	manjunath	25	male	278772	<130u/l	>4850 u/l	mild	no
38	robert	32	male	278772	>130u/l	>4850 u/l	severe	yes
39	venkataramareddy	62	male	279633	<130u/l	>4850 u/l	mild	no
40	pratap	22	male	283774	<130u/l	<4850 u/l	mild	no
41	balaraju	25	male	293775	<130u/l	>4850 u/l	mild	no
42	srinath	24	male	294720	<130u/l	<4850 u/l	mild	no
43	suman	22	male	299290	<130u/l	>4850 u/l	mild	no
44	rekha	25	female	404147	>130u/l	>4850 u/l	mild	no
45	divya	31	female	405939	<130u/l	>4850 u/l	mild	no
46	chinnamma	62	female	414939	>130u/l	>4850 u/l	mild	no
47	pavithra	25	female	360343	<130u/l	>4850 u/l	mild	no
48	roopa	25	female	365983	>130u/l	<4850 u/l	severe	yes
49	achamma	60	female	368630	<130u/l	>4850 u/l	mild	no

50	asha	18	female	372439	>130u/l	<4850 u/l	severe	yes
51	susheelamma	30	female	405123	<130u/l	>4850 u/l	mild	no
52	chandrashekar	30	male	300394	<130u/l	<4850 u/l	moderate	yes
53	srinath	25	male	301981	<130u/l	>4850 u/l	moderate	yes
54	nalini	20	female	379842	<130u/l	>4850 u/l	mild	no
55	kavitha	38	female	382299	>130u/l	>4850 u/l	mild	no
56	susheela	35	female	395605	<130u/l	>4850 u/l	mild	no
57	anusha	30	female	429903	>130u/l	>4850 u/l	severe	yes
58	chethan	23	male	301981	<130u/l	>4850 u/l	mild	no
59	ramesh	38	male	307562	<130u/l	<4850 u/l	mild	no
60	ambrish	31	male	315936	<130u/l	>4850 u/l	mild	no
61	narayanswamy	45	male	321136	<130u/l	<4850 u/l	mild	no
62	venkatesh	24	male	323935	<130u/l	>4850 u/l	mild	no
63	suresh	25	male	343119	>130u/l	<4850 u/l	moderate	yes
64	khaleen	35	male	344831	>130u/l	<4850 u/l	moderate	yes
65	srimathi	23	female	441181	>130u/l	<4850 u/l	mild	yes
66	nagarathnamma	26	female	444126	>130u/l	<4850 u/l	severe	yes
67	varalakshmi	23	female	445972	>130u/l	<4850 u/l	mild	yes
68	anitha	27	female	448444	<130u/l	>4850 u/l	mild	no
699	ravi	35	male	385573	>130u/l	<4850 u/l	severe	yes
70	venkataramappa	50	male	335760	<130u/l	>4850 u/l	mild	no
71	avin	25	male	337549	<130u/l	<4850 u/l	mild	no
72	krishnamurthy	25	male	339996	>130u/l	<4850 u/l	severe	yes
73	papanna	60	male	340488	>130u/l	<4850 u/l	severe	yes
74	venkateshppa	55	male	342169	>130u/l	>4850 u/l	moderate	no
75	rekha	25	female	404147	>130u/l	<4850 u/l	moderate	yes
76	divya	31	female	405123	<130u/l	>4850 u/l	mild	no

77	chinnamma	62	female	405939	>130u/l	<4850 u/l	mild	yes
78	sandhya	36	female	403458	<130u/l	>4850 u/l	mild	no
79	muniraju	24	male	326306	<130u/l	>4850 u/l	mild	no
80	ramesh	55	male	329840	<130u/l	<4850 u/l	mild	no
81	prabhakar	26	male	333514	<130u/l	>4850 u/l	mild	no
82	rajendra	25	male	333936	<130u/l	>4850 u/l	mild	no
83	subbalakshmi	26	female	332068	>130u/l	<4850 u/l	mild	no
84	ravinath singh	35	male	347720	<130u/l	<4850 u/l	mild	no
85	subramani	45	male	345686	<130u/l	>4850 u/l	mild	no
86	nagabushan	30	male	354475	>130u/l	>4850 u/l	severe	yes
87	mahendra	29	male	351925	>130u/l	>4850 u/l	mild	no
88	ramanna	65	male	360772	<130u/l	>4850 u/l	mild	no
89	krishna	35	male	359279	>130u/l	<4850 u/l	severe	yes
90	sandeep	38	male	361437	<130u/l	>4850 u/l	mild	no
91	anjinappa	32	male	376564	>130u/l	>4850 u/l	moderate	yes
92	vashnathkumar	25	male	376957	<130u/l	<4850 u/l	mild	no
93	sandhya	36	female	403458	<130u/l	<4850 u/l	mild	no
94	manjunath	36	male	386239	>130u/l	<4850 u/l	mild	yes
95	seetharam	28	male	400783	<130u/l	<4850 u/l	moderate	no
96	munikrishna	43	male	400783	>130u/l	>4850 u/l	severe	yes
97	venkatareddy	64	male	405947	<130u/l	<4850 u/l	mild	no
98	karthy	28	male	418904	<130u/l	<4850 u/l	mild	no