PREDICTORS OF SEVERITY AND OUTCOME

IN ACUTE ORGANOPHOSPHORUS POISONING

By

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LIST OF ABBREVIATIONS

ABG	→	Arterial Blood Gas
Ach	→	Acetyl Choline
AChE	→	Acetyl Cholinesterase
ACTH	→	Adrenocorticotropic Hormone
ANS	→	Autonomic Nervous System
APACHE	→	Acute Physiology and Chronic Health Evaluation
AST	→	Aspartate Aminotransferase
ATP	→	Adenosine Triphosphate
BChE	→	Butryl Cholinesterase
CNS	→	Central Nervous System
COPIND	→	Chronic Organophosphate Induced Neuropsychatric Disorder
CPK	→	Creatinine Phosphokinase
DDT	→	Dichloro Diphenyl Trichloroethane
DDVP	→	Dichlorovas
ECG	→	Electrocardiograph

EPN	→	-o, ethyl-o-p nitrophenyl benzene thionophsophate
GCS	→	Glasgow Coma Scale
HOD	→	Head of the Department
HT	→	Head Trauma
ICU	→	Intensive Care Unit
IMS	→	Intermediate Syndrome
IPCS PSS	→	International Program on Chemical Safety - Poison Severity Score
LD50	→	Lethal Dose 50
LDH	→	Lactate Dehydrogenase
NE	→	Norepinephrine
NMJ	→	Neuromuscular Junction
NTE	→	Neuropathy Target Esterase
OMPA	→	Octamethyl Pyrophoramide
OP	→	Organophosphorous
OPC	→	Organophosphorous Compound
OPIDN	→	Organophosphorous Induced Delayed Neuropathy

OPP	→	Organophosphorous Poisoning
PAM	→	Pralidoxime
PSS	→	Poisoning Severity Score
RBC	→	Red Blood Cell
SDUMC	→	Sri Devraj Urs Medical College
TEPP	→	Tetraethyl pyrophosphate
WHO	→	World Health Organization

ABSTRACT

BACKGROUND AND OBJECTIVES: Organophosphorous compound poisoning is the most common medico-toxic emergency in India. Respiratory failure is the most common complication of OP poisoning leading to death. Early recognition and prompt ventilatory support may improve survival. Owing to limited availability of resources, all OP poisoning patients are not managed in ICUs in Indian setup. It is therefore important that clinical features and criteria to predict the need for ventilatory support be identified at initial examination. Hence, this study was undertaken to predict the severity and outcome of acute organophosphorous compound poisoning.

METHODOLOGY: 55 cases of acute OPC poisoning admitted to R. L. Jalappa Hospital attached to SDUMC, Tamaka, Kolar between February 2011 and February 2012 were studied. Patients above 18 years of age were included and those patients with mixed poisoning were excluded. Detailed history and clinical examination was undertaken according to the proforma with special reference to the need for ventilatory support. Severity on admission was assessed using GCS, PSS and APACHE III scoring systems. The results were analyzed using chi-square test.

RESULTS: The average age at presentation was found to be 28.33 years. 54.5% of the patients were in the 21-30 age group. Majority of the patients in the study were found to be males. Majority of the patients were agriculturists by profession and next was the students. The most common organophosphorous compound consumed was Chlorpyriphos. Approximately, 75% of the patients had a GCS between 13-15

at presentation. 47.3% of the cases were found to have mild PSS. The average APACHE score was 43.81. 81.8% of the patients had a score of less than 60. 16.4% of the patients were found to have a positive Troponin T on admission. 69 % had an elevated CKMB on admission and 31% had normal values on admission. 63.6% of the patients had normal sinus rhythm on admission. 58% of the patients had a Pseudocholinesterase level of less than 1000 on admission. 20% of the patients required intubation and subsequent ventilator support. The mean ICU length of stay was 6.15 days. In our study, 94.6% of the patients recovered completely and only one patient succumbed.

CONCLUSIONS: Low GCS scores, severe PSS and high APACHE scores significantly predicted severity. A low pseudocholinesterase level on day 7 is a significant marker of severity. Low levels on admission also predicts probable need of ventilation and need for prolonged duration of atropine administration. In our study, blood sugar levels, serum amylase levels, CPK and ABG analysis did not predict prognosis. Positive troponin T levels, elevated CKMB levels and tachycardia are markers of cardiotoxicity and significantly predict severity of poisoning. Other factors which influence severe poisoning are ingestion of chlorpyriphos or cypermethrin; delayed presentation of > 5 hours. A delayed pre-hospitalization period (>5 hours) was found to have a definite association with mortality.

KEYWORDS: Organophosphorous, Scoring System, Pseudocholinesterase, Cardiotoxicity.

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INTRODUCTION

Organophosphorous compound (OPC) poisoning has assumed alarming proportions with an annual incidence of over 3 million patients in 1990. Organophosphorous compound poisoning is primarily a problem of the developing countries.[1] Organophosphorous compound poisoning is the most common medico toxic emergency in India. Acute Organophosphorous compound poisoning is an important indication for emergency admission in most hospitals throughout India.[2]

Organophosphorous compounds were first developed by Schrader shortly before and during the Second World War. They were first used as an agricultural insecticide and later as potential chemical warfare agents.[2] Organophosphorous (OP) compounds are used as pesticides, herbicides, and chemical warfare agents in the form of nerve gases.[2] Its widespread use and easy availability has increased the likelihood of poisoning with these compounds.

India is a predominantly agrarian country with about 60-80% of rural population. Pesticides are routinely used for advanced farming and they are readily available over the counter. Therefore, a pesticide is an easy access source for the suicidal purpose.[3]

They have been imported in India since 1951, but very few knew the nature of these compounds as a virulent poison till the Kerala food poisoning tragedy in 1958. This tragedy took a toll of hundred and odd due to inadvertent stocking of food stuff and

folidol packages in the same hold where the folidol containers leaked and contaminated the gunny bags containing food stuff.[4]

The WHO estimates that approximately 3 million pesticide poisonings occur annually worldwide and cause more than 220,000 deaths. Developing countries like India and Sri Lanka report alarming rates of toxicity and death.[4]

Organophosphates act by irreversibly inhibiting the enzyme cholinesterase, resulting in accumulation of acetylcholine at synapses and myoneural junctions leading to cholinergic over activity. Direct cardio toxic effect of organophosphorous compounds is also reported.[5,6,7]

Mortality ranges from 4-30% in Indian studies. Respiratory failure is the most common complication of OP poisoning leading to death. Early recognition and prompt ventilatory support may improve survival. Owing to limited availability of resources, all OP poisoning patients are not managed in ICUs in Indian setup. It is therefore important that clinical features and criteria to predict the need for ventilatory support be identified at initial examination.

Serum cholinesterase levels are easier to estimate and usually depressed after OP poisoning. GCS, PSS and APACHE III are commonly used scoring systems in the ICU. These could be used as simple and effective systems to determine the need for ventilatory support early on in the course.

Hence, this study was undertaken to assess the factors which may be used as tools to predict the severity and to assess outcome in acute organophosphorous compound poisoning both clinically by using scoring systems and by estimating serum cholinesterase levels, analyzing cardiotoxicity and other metabolic parameters.

OBJECTIVES OF THE STUDY

- To identify the factors, which help in predicting the severity on admission, in patients with organophosphorous compound poisoning.
- To identify factors which help in predicting outcome in patients with organophosphorous poisoning.

REVIEW OF LITERATURE

ORGANO-PHOSPHORUS COMPOUND POISONING

Organophosphorous compounds and carbamates that were first discovered more than 100 years ago, are at present the predominant groups of insecticides employed globally for pest control. The compounds are toxic to humans and represent a source of poisoning domestically, in some occupation or when ingested as a suicidal agent.[8]

During the past four decades, more than 35,000 different formulations have come into use as pesticides.[9] Of these, organophosphorous insecticides are possibly the most widely used in the world.

Modern investigations of organophosphorous compound date from 1932 when Lange and Krugger recorded the synthesis of dimethyl & diethyl phosphor-fluoridates. They noted that these compounds caused a persistent choking sensation and blurring of vision. This observation led Schrader of I.G. Farben industries to develop organophosphorous compound, first as agricultural insecticides and later as potential chemical warfare agents.

Consequently, during World War II, several toxic compounds were developed and used as nitrogen gases in Germany.[10]

In 1991, these very compounds formed the cornerstone of Iraq's much-dreaded chemical warfare arsenal during the Gulf war.

Organophosphorous compound first came to India in 1951, to be used as insecticides and in 1962, the first Organophosphorous poisoning was reported in India.[11]

SOURCES OF OP PESTICIDES[1]

The organophosphates have achieved great popularity because of their effectiveness as insecticides and their lack of persistence in the environment. As they have an unstable chemical structure, they disintegrate into harmless radicals within days of application. They do not persist in the body or environment, as do DDT and other organochlorides. Hence, they have replaced DDT as insecticide agent of choice. The principal use of these compounds is as pesticides in agriculture, mainly as insecticides. Some formulations are used as veterinary and human medicine. In commerce organophosphorous compounds have been used as lubricants, plasticizers and flame retardants. The development and use of some of these compounds as very potent agents of warfare is of global significance.

Table 1: Source of OP Agents

Domestic
• Garden sheds—in particular insecticidal preparations but also other products that are marketed as fertilizers but contain some organophosphorus pesticides, available as solid or liquid formulations
• Surface and room sprays
• Baits for cockroaches and other insects (for example, chlorpyrifos)
• Shampoos against head lice (for example, malathion)
• Pet preparations (for example, pet washes, collars)
Industrial or occupational
• Crop protection and livestock dipping
• Large scale internal control, including fumigation
Terrorism or warfare (nerve agents)

FUNCTIONAL ORGANIZATION OF THE AUTONOMIC NERVOUS SYSTEM

The portion of the nervous system which controls the visceral functions of the body is called the autonomic nervous system. This helps in control of arterial pressure, gastrointestinal motility, secretions, urinary bladder control, sweating, and body temperature etc. ANS centers are located in the hypothalamus, brain stem and spinal cord.

Sympathetic

- Spinal cord : T1 - L1
- Prevertebral ganglia - coeliac and hypogastric

Parasympathetic

- From CNS - III, VIII, IX, X cranial nerves
- Spinal cord - S2, S3, S4 nerves.

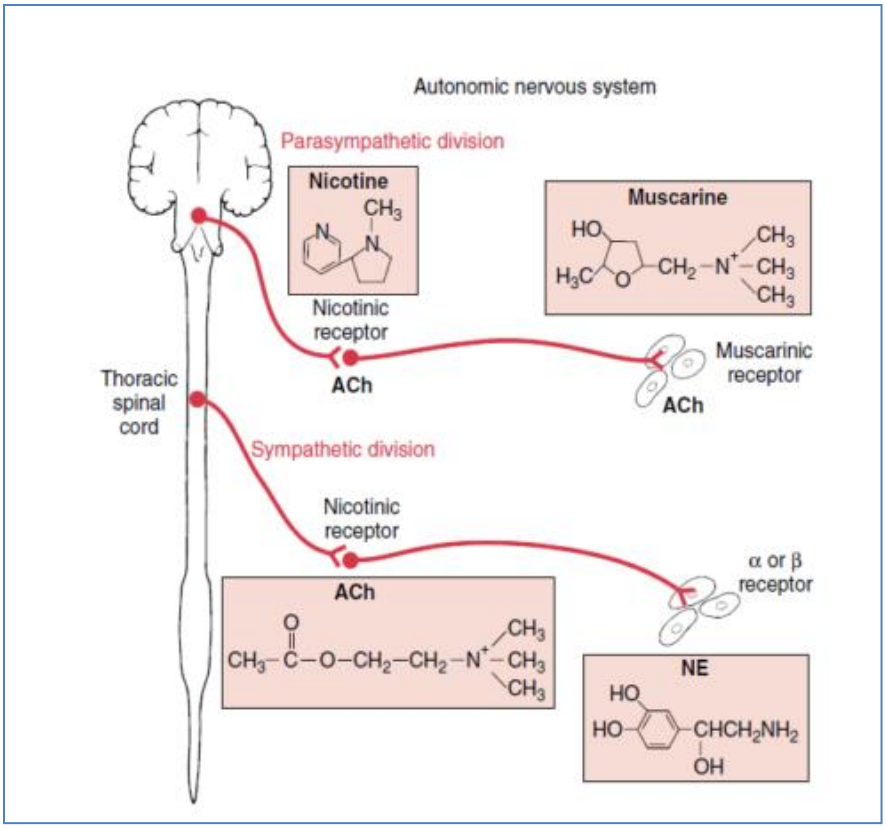


Figure 1: Neurochemistry of Autonomic Nervous System

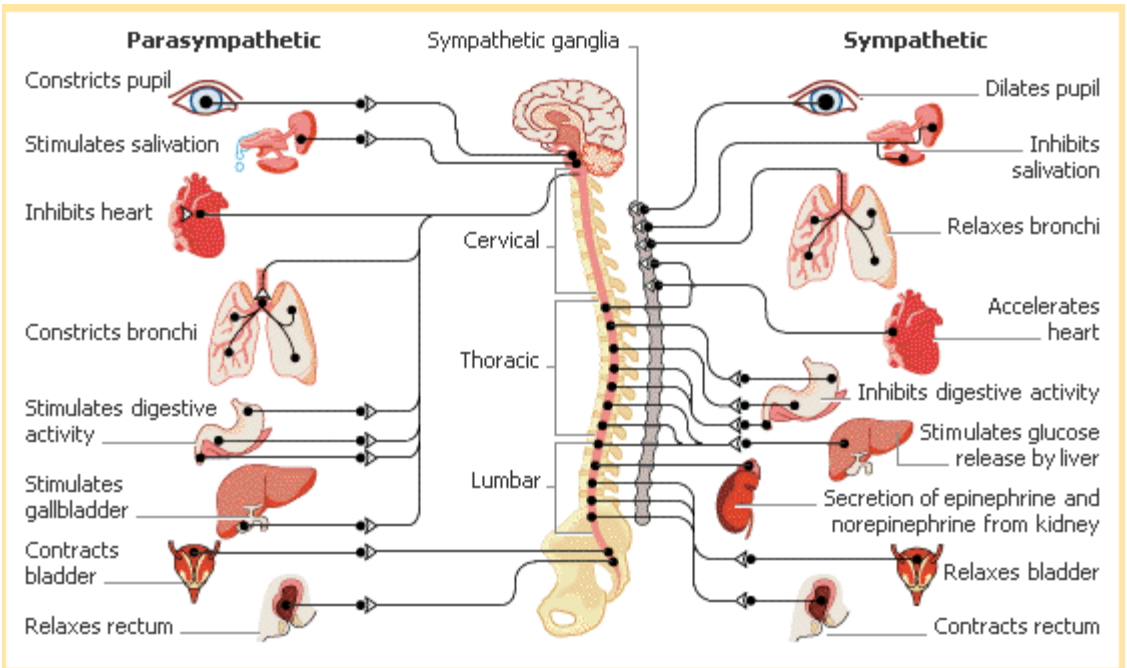


Figure 2: Organ Specific Arrangement of ANS

Neurotransmitters[12,13]

1. Nor-epinephrine (NE) is the neurotransmitter of the [re-ganglionic sympathetic neurons and hence they are called as "adrenergic".
2. At the preganglionic neurotransmission, acetyl choline is the neurotransmitter for both divisions of the ANS as well as the post-ganglionic neurons. Hence, they are called as "Cholinergic" neurons.

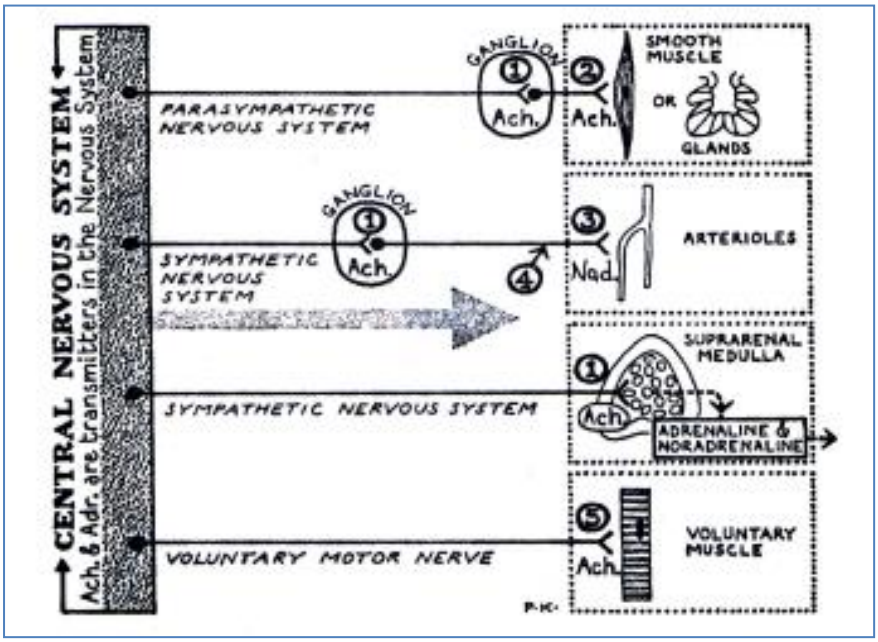


Figure 3: Sites of Action of Neurotransmitters

ACETYL CHOLINE

Acetyl choline (Ach), first synthesized by Bayer in 1867, is a neurotransmitter. It was first recognized as a potent pharmacological substance by Hunt in 1906.

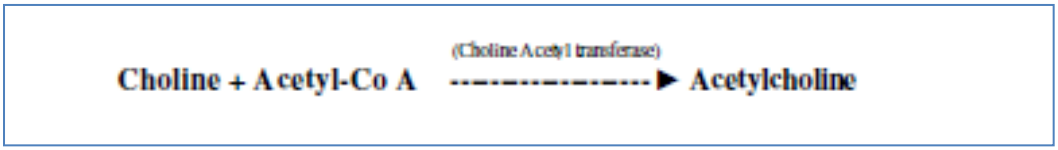
Acetylcholine is produced at

a. Autonomic effector sites innervated by post-ganglionic parasympathetic fibres.

b. Pre-ganglionic autonomic fibres of sympathetic and parasympathetic ganglion cells and adrenal medulla.

c. Motor end plates on skeletal muscle.

d. Certain synapses in CNS.



The Ach in the motor nerve terminal is synthesized in the axoplasm from choline and CoA by a process facilitated by the enzyme Choline Acetyl Transferase. The choline necessary for this is derived from ECF which is transported into the nerve terminal by a carrier mediated transport system.

About 20% of Ach in the nerve terminal is present as free Ach in the axoplasm, and 80% is contained within the vesicles, each containing about 4-5 x 10^5 molecules of Ach.

Separate pools or stores of Ach exist within the nerve terminal. Most of the Ach (80%) can be released by nerve imoulses (the releasable pool), but some cannot (the non-releasable pool or the stationary pool). The releasable pool consists of the Ach contained

within the vesicles, whereas the non-releasable pool is the Ach of the axoplasm. Releasable pool is often divided into immediately available and the reserve pool.

Acetyl choline acts through two receptors:[12,13]

1. **MUSCARINIC RECEPTORS**: *Muscarine* is a poison from toad stools that activates only muscarinic receptors. Effector cells are stimulated by post ganglionic neurons of the parasympathetic nervous system and also postganglionic cholinergic neurons of the sympathetic nervous system.
2. **NICOTINIC RECEPTORS**: Nicotine will activate the nicotinic receptors in pre and post ganglionic neurons of both the sympathetic and parasympathetic nervous systems and also in the membranes of skeletal muscle fibers at NMJ.

Metabolism of Acetyl choline

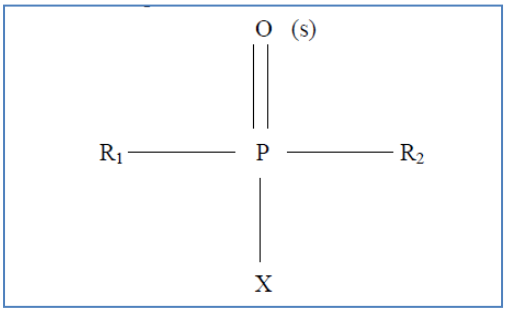
Junctional acetyl cholinesterase is the enzyme responsible for the hydrolysis of Ach in the synaptic cleft.

Acetyl cholinesterase is a protein attached to the basement membrane of the muscle and probably also the membranes of the motor end plates and the nerve terminals. Each molecule of the enzyme is able to bind and hydrolyze several molecules of Ach. It has been estimated that for each molecule of Ach released by a nerve imoulse, there are atleast 20 active enzymes available. This arrangement ensures that each Ach molecule only reacts with the receptor, after which it is rapidly hydrolysed (< 1 msec).[2]

CHEMISTRY

Organophosphorous compounds are usually esters/amides of thiol derivatives of phosphoric / phosphonic acids.

The General formula being:



Where,

- R1 and R2 are usually simple alkyl or aryl groups.
- X is known as the "leaving group" may be one of a wide variety of substituted or branched aliphatic, aromatic or heterocyclic groups linked to phosphorous via a bond of some liability usually –O-or -S-.
- The double bonded atom may be O or S & the related compound, termed a phosphate or phosphorothioate.

Organophosphorous compounds are degradable organic compounds containing carbon–phosphorus bonds (thus excluding phosphate and phosphite esters, which lack this kind of bonding), used primarily in pest control as an alternative to chlorinated hydrocarbons that persist in the environment.

Phosphorus shares group 5 in the periodic table with nitrogen and phosphorus compounds and nitrogen compounds are somewhat related.[14,15,16] Phosphorus can adopt a variety of oxidation states, and it is general to classify organophosphorous compounds based on their being derivatives of phosphorus(V) versus phosphorus(III), which are the predominant classes of compounds. In a descriptive but only intermittently used nomenclature, phosphorus compounds are identified by their coordination number δ and their valency λ. In this system, a phosphine is a $\delta^3\lambda^3$ compound.

CLASSIFICATION

Holmstedt proposed a classification system for organophosphorous that is of pharmacological and toxicological interest. The compounds are divided into 5 groups with a few relevant examples.[10]

GROUP	X	EXAMPLES
A	Halogen, Cyanide & Thiocyanate	Disopropylophosphate flourdate (DFP) , ISO propyl methyl phosphoflouridate (SARIN), Pinacolyl Methyl phosphoflouridate (SOMAN)
B	Alkyl, alkoxy, aryloxy	Forstenon, DDVP, Pyrazoxon
C	Thiol or Thiophosphorous Compound	Parathion, Malathion, Azethion, Diazinon, Systox, and Demeton
D	Pyrophosphates and related compounds	TEPP, DPDA, OMPA
E	Quaternary Ammonium Compound	Phospholin

An older more commonly used classification divides these compounds into: 1) Alkyl phosphates (E.g. TEPP, HETP, OMPA, Malathion, Systox, DFP etc). 2) Aryl Phosphates (E.g. Demeton, Parathion, EPN, Chlorothion, Diazinon, etc).

TOXICITY[17]

The toxicity of OPCs varies widely, based on the specific agent, the route and duration of exposure, and potent specific factors such as genetic differences in OP metabolism and enzyme susceptibility to the agent. The most potent OP compounds are those that have been developed by chemical weapons (E.g.: sarin, soman, tabun,VX).[18] Commercial agricultural OP products also have a high toxicity. Animal and household OP products are typically much less potent. As agents relative toxicity to is generally expressed as a measurement of its lethal dose in experimental animals (LD50).

Table 2: Trade and generic names and WHO classification of OP and carbamate poisons implicated in poisoning

S.No	Trade names	Chemical name	WHO Class
	Organophosphates		
1.	Unknownsuspected OP poison	-NA-	-
2.	Metacid, Folidol	Methyl parathion	Ia
3.	Phoskil, Nuvacron, Monophos	Monocrotophos	Ib
4.	Ekalux	Quinalphos	II
5.	Rogur 30 E, Crogor	Dimethoate	II
6.	Lethal, piridane	chlorpyriphos	II
7.	Thimet, Phorate	Phorate	Ia
	Carbamates		
8.	Baygon, Hit	Propoxur	II
9.	Furadan, Carburan	Carbofuran	Ib
10.	Sevin	Carbaryl	II
	Unknown pesticide		-
	Total		

Ia – Extremely hazardous

Ib – Highly hazardous

II – Moderately hazardous

III – Slightly hazardous

PHARMACODYNAMICS AND METABOLISM

These compounds are generally dispersed as aerosols/dusts, consisting of organophosphorous compound absorbed to an inert finely particulate material. Therefore, practically all routes including gastrointestinal tract, skin and mucous membranes following contact with the liquid form, rapidly and effectively absorb these compounds.

The lungs also absorb them, after inhalation of the vapors or finely dispersed dusts/ aerosols. Following absorption they quickly distribute in all tissues, maximum concentration usually being reached in the liver and the kidneys. Lipophilic compounds may reach high concentration in neural and other lipid rich tissues.

Plasma half-life ranges from few minutes to few hours, depending on the compounds and route of administration.

Metabolism occurs primarily by oxidation - *PARATHION* is converted to biologically active compound – "Paroxon" in the liver.

MALATHION is metabolized to inactive compound more rapidly in higher animals, and consequently is less dangerous to man.

Highly lipid soluble agents- *CHLORFENTHION* may produce symptoms and signs of cholinergic over activity for an extended period of days to weeks, caused by subcutaneous lipid storage followed by subsequent chronic systemic release after redistribution. These compounds also cause repeated release after apparently successful management.

Detoxification of the organophosphorous insecticides occurs, either by bio-chemical modification of their structure or by linkage to the binding site without toxicological significance.

Elimination of organophosphorous compounds and their metabolites occur mainly through urine and faeces, with 80-90% of most of compounds being eliminated within 48 hours. A very small portion of organophosphorous compounds and their active forms are excreted unchanged in the urine. Some compounds are known to persist in the body for longer periods like Fenthion and Fenithrothion.

MECHANISM OF ACTION

Anticholinesterases bind to and inhibit a number of enzymes, yet it is their action on the esterase which is of clinical importance.[19]

a. Inhibition of Acetylcholinesterases (AchE)

Acetylcholinesterases (AchE) are responsible for the hydrolytic cleavage of Acetylcholine (Ach) to choline & acetic acid. Acetylcholine is a neurotransmitter for all postganglionic autonomic fibers, postganglionic parasympathetic fibers, postganglionic sympathetic fibers, neuromuscular junction and some interneuron synapses in the CNS. A potential reaction causes release of acetylcholine in the presynaptic cleft, most of which is degraded by acetyl cholinesterase. Acetylcholine, which is not degraded, binds to the postsynaptic receptors resulting in the generation of an excitatory postsynaptic potential and propagation of the impulse. Anti-acetyl cholinesterase has two sites namely, anionic and esteratic site. Acetylcholine binds to the anionic site on acetyl cholinesterase and

undergoes hydrolysis in a few seconds. The reversible Anti-acetylcholinesterase combine with acetylcholinesterase at the anionic site and this blocks attachment of the substrate.[20]

Irreversible Anti-acetylcholinesterases on the other hand binds to the esteratic site of the Acetylcholine and inhibit irreversibly thereby phosphorylating it. This leads to accumulation of acetylcholine at the synapses with initial overstimulation followed by inhibition of synaptic conduction. Following inhibition, reactivation of the enzyme (acetylcholinesterase) occurs at the rate of 1% per day by slow de novo synthesis of fresh enzyme and also by spontaneous dephosphorylation.[21]

The rate of inactivation (phosphorylation) and reactivation (dephosphorylation) depends of the species and the tissue in addition to the chemical group attached accounting for the differences in toxicity.[22]

Response to reactivating agents decline with time, a process referred to as '*AGING*' of the inhibited enzyme. It is a result of loss of an alkyl or alkoxyl group leaving a much more stable mono-alkyl or mono-alkoxyl phosphoryl acetylcholinesterase.[23] The aged phosphorylated enzyme cannot be reactivated by oximes.[24] In chemical warfare agents like Soman, aging occurs rapidly.[21]

b. Neuropathy target esterase inhibition

Neuropathy target esterase (NTE) is an integral membrane protein present in all neurons and in some non-neural-cell types of vertebrates. Recent data indicate that NTE is involved in a cell-signaling pathway controlling interactions between neurons and accessory glial cells in the developing nervous system.

NTE comprises at least two functional domains: an N-terminal putative regulatory domain and a C-terminal effector domain which contains the esterase activity and is, in part, conserved in proteins found in bacteria, yeast, nematodes and insects. NTE's esterase activity appears to be largely redundant in adult vertebrates, but organophosphates which react with NTE in order to initiate unknown events which lead, after a delay of 1±3 weeks, to a neuropathy with degeneration of long axons. These neuropathic organophosphates leave a negatively charged group covalently attached to the active-site serine residue, and it is suggested that this may cause a toxic gain of function in NTE.

Neuropathy target esterase inhibition (NTE) followed by its transformation to an aged form is responsible for the organophosphate- induced delayed neuropathy (OPIDN).[25]

PATHOPHYSIOLOGY

OPCs are cholinesterase inhibitors and exert their toxicity by interfering with the normal function of Ach, an essential neurotransmitter throughout the autonomic and central nervous system.

Organophosphates are powerful inhibitors of corboxylic ester hydrolases including chymotrypsin, acetylcholinesterase, plasma or butyryl cholinesterase (pseudocholinesterase), plasma and hepatic carboxylesterase (aliesterases), paraoxonases (A.esterases), and other nonspecific proteases. Functioning acetylcholinesterase is found in human nervous tissue and skeletal muscles and is also genetically expressed on the membrane of erythrocytes.

The active acyl pocket in the center of acetylcholinesterase is a narrow cleft 2 nm deep and surrounded by tetramers. Two additional domains on the enzyme include a peripheral anionic site and a choline subsite of the active center. These three sites confer the stereo-specificity for other ligands to bind. At the base of the cleft, the enzymatic active site contains a serine 203 residue. Coiled nearby are a histidine 447 residue and a glutamate 334. When Ach enters the binding area, it is attracted by local atomic forces into a tetrahedral structure with the serine, histidine and glutamate, and forms a nucleophilic serine hydroxyl intermediate. The acetylcholine is hydrolysed to acetic acid and choline, which then leaves the site and enzyme, and reforms its allosteric structure. Turnover time for this reaction is 130 microseconds.[26]

Although organophosphorous compounds differ structurally from Ach, they can bind to the acetylcholinesterase molecule at the active site and phosphorylate / phosphonate the serine moiety. When this occurs, the resultant conjugate is infinitely more stable than the acetylcholine-acetylcholinesterase conjugate, although endogenous hydrolysis does occur. Depending upon the amount of stability and charge distribution, the time to hydrolysis is increased. Phosphorylated or phosphorylated enzymes, degrade

over days to weeks, making the acetylcholinesterase essentially inactive. In order for the physiologic enzyme activity to return, new enzyme must be generated or antidote given.[27]

Once the acetylcholinesterase is phosphorylated, over the next 24 to 48 hours, an allyl group is eventually lost from the conjugate, further exacerbating the clinical situation. As this, ageing, occurs, the enzyme can no longer spontaneously hydrolyze and is permanently inactivated.[26]

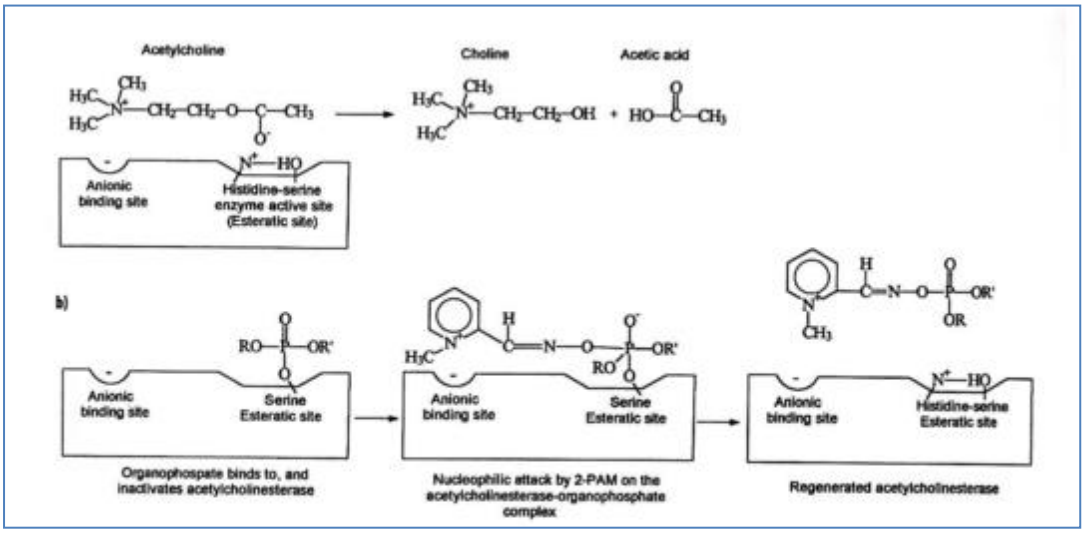


Figure 4

(a) Hydrolysis of Acetylcholine by Acetylcholinesterase.

(b) Reactivation of Alkyl phosphorylated Acetylcholinesterase.[28]

CLINICAL FEATURES

The clinical manifestations of organophosphorous poisoning are a result of cholinergic over activity and can be divided into the effects of over stimulation of the muscarinic, nicotinic and CNS receptors.[8]

Table 3: Common effects of acute OPC toxicity based on receptors

Muscarinic	Nicotinic	Central
Miosis	Muscle Fasciculations	Unconsciousness
Blurred vision	Paralysis	Confusion
Nausea	Pallor	Toxic psychosis
Vomiting	Muscle weakness	Seizures
Diarrhoea	Hypertension	Fatigue
Salivation	Tachycardia	Respiratory Depression
Lacrimation	Mydriasis (rare)	Dysarthria
Bradycardia		Ataxia
Abdominal pain		Anxiety
Diaphoresis		
Wheezing		
Urinary Incontinence		
Fecal Incontinence		

The clinical diagnosis is based on:

- History of exposure
- Presence of several of the above symptoms and signs.

The time interval between the exposure and onset of symptoms and signs varies with the route and degree of exposure. The interval maybe within 5 minutes after massive ingestion and is almost always less than 12 hours. The severity of manifestation varies with the degree of poisoning.

Namba et al[29] have made a classification of organophosphorous poisoning insecticide which is modified from Grob et al[30] and is as follows:

- **Latent Poisoning**: No clinical manifestations are seen. Diagnosis based on estimation of serum cholinesterase activity, which is inhibited by 10 to 50%.

- **Mild Poisoning**: The patient complains of fatigue, headache, dizziness, nausea, vomiting, excessive sweating, salivation, abdominal cramps or diarrhea. Serum cholinesterase levels are 20- 50% of normal values.
- **Moderate Poisoning**: The patient complains of generalized weakness, difficulty in talking, muscular fasciculations and miosis. Serum cholinesterase levels are 10-20% of normal values.
- **Severe Poisoning**: Marked miosis, loss of pupillary reflex to light, muscular fasciculation, flaccid paralysis, and secretions from the mouth and nose, rales in the lungs, respiratory difficulty and cyanosis are seen in patients with severe poisoning. Serum cholinesterase levels are lower than 10% of normal values.

However, this proposed grading has proved unworkable in clinical practice because of many varied clinical criteria in different grades, as well as the difficulty in remembering and applying them in acute clinical situation.[8,31]

The second classification was proposed by Bardin et al[31] and is as follows:

- **Grade 0**: Positive history, no signs of organophosphorous poisoning.
- **Grade 1:** Mild secretions, few fasciculations and normal level of sensorium.
- **Grade 2:** Copious secretions, Generalized fasciculation, Rhonchi, crepitations, Hypotension (systolic BP <90mmHg) Disturbed level of consciousness and not stuporous.
- **Grade 3:** Stupor, PaO_2 < 50mmHg, Chest roentgenogram abnormal.

This study by Bradin et al showed that patients with grade 3 manifestations on admission were associated with increased requirement for mechanical ventilator. The presence of other complications and increased days of ICU stay have been observed in the above patients.

Following organophosphorous poisoning three well-defined clinical phases[719] are seen:

- Initial acute cholinergic crisis
- The intermediate syndrome
- Delayed Polyneuropathy (OPIDN-Organophosphorous Induced Delayed Neuropathy)
- Chronic Organophosphate Induced Neuropsychatric Disorder (COPIND).

1. Acute cholinergic phase

This is the initial phase of acute poisoning resulting in muscaranic and nicotinic effects.

- The accumulation of acetylcholine at the muscarnic site produces an increase in secretions. Bronchorrhea, salivation, sweating, bradycardia, vomiting and an increase in gastro-intestinal motility (abdominal tightness and cramps) are commonly seen. In the eye, organophosphorous agents cause the diagnostic miosis which results in blurring of vision.

- The effects of increased acetylcholine at nicotinic sites [E.g.: The neuromuscular junction] cause muscle fasciculation. Inhibition of acetylcholinesterase in the brain leads to headache, insomnia, giddiness, confusion and drowsiness. After severe exposure, slurred speech, convulsions, respiratory depression and coma occur.
- The mechanism of action of paralysis is depolarization and desensitization blocks induced by acetylcholine at the neuromuscular junctions.
- Death is likely during this initial cholinergic phase due to effects on the heart like bradycardia, arrhythmias; respiratory failure and depression of vital centers in the brain. Bradycardia may be severe and may progress to heart block.

The cholinergic phase usually lasts 24 to 48 hours and constitutes a medical emergency that required treatment in an ICU.[21]

2. Intermediate syndrome

Senanayake and Karallieda first coined the term "Intermediate Syndrome" in 1987.[32] After recovery from the cholinergic crisis, but before the expected onset of delayed polyneuropathy, some patients develop a muscle paralysis, which is described as Intermediate syndrome. This phenomenon has been reported in between 20-68% of the patients.[33]

The cardinal feature of this syndrome is muscle weakness affecting predominantly the proximal limb muscle and neck flexors. Motor cranial nerve palsies (III to VII and X) also occur. Respiratory muscle weakness leading to respiratory failure could lead to a fatal outcome. Deep tendon reflexes are usually depressed. The intermediate syndrome occurs after recovery from the cholinergic crisis within 24 hours to 96 hours but before the expected onset of the delayed neuropathy, which occurs 2 to 3 weeks after the poisoning.[4]

Complete recovery occurs within 4 to 18 days, if adequate ventilator support is provided. But, altered function at the NMJ may persist upto 2 years after its occurrence. The agents commonly responsible are Fenthion, Monocrotophos, Dimethoate, Diazinon and Methyl Parathion.[34]

A consensus from literature search shows that:

- IMS may result from inadequate therapy with oximes.
- The symptom complex begins at a time when cholinesterase function is very low and the OP compound is still detectable in the body.
- As blood levels of OPCs fall and OPCs tissue redistribution occurs, the motor end-plate may be rechallenged by the cholinesterase inhibitor in the presence of inadequate circulatory oximes.

3. Organophosphorous Induced Delayed Polyneuropathy (OPIDP)

The neuropathy develops following latent periods of 2-4 weeks after the cholinergic crisis. The cardinal symptoms are distal muscle weakness, calf pain preceding the weakness and in some cases paraesthesia in the distal parts of the limbs. Weakness initially appears in the leg muscles causing foot drop, followed by small muscles of the hands. Later it may extend proximally and may even involve the truncal muscles. Deep tendon jerks are absent. The prognosis of patients with mild neuropathy is good but those with severe neuropathy are usually left with persistent deficits that are claw hand, foot drop, persistent atrophy, spasticity and ataxias.

Delayed polyneuropathy is common following exposure to organophosphorous compounds, which have weak anticholinesterase activity E.g. Triortho-cresyl-phosphate. The occurrence of Delayed Polyneuropathy appears to follow phosphorylaion and subsequent aging of an enzyme in axons called as *Neuropathy Target Esterase* (NTE). The function of this enzyme is not clear yet. It is however present in the brain, spinal cord and the peripheral nervous system. NTE is a membrane bound protein with high esterase catalytic activity. This phosphorylaion enzyme also undergoes ageing.[35] The agents commonly responsible are Mepafox and Chloropyrifos.[36,37,38,39]

Table 4: Comparison of IMS and Opidn

Variable	Intermediate syndrome	Delayed polyneuropathy
Time of onset after poisoning	1-4days	2-3weeks
Sites of weakness Limb muscles Neck muscles Cranial nerves Respiratory muscles	 Proximal + + +	 Distal - - -
Electromyogram	Titanic fade	Denervation
Recovery, from time of onset	4-18days	6-12months
OPs commonly involved	Fenthion Dimethoate Monocrotophos	Methamidophos Trichlorfon Leptophos

3. **Chronic Organophosphate Induced Neuropsychiatric Disorder (COPIND)**

Behavioral effects have been documented following acute or chronic organophosphorous poisoning. These include:

- Impairment of vigilance, information processing, psychomotor speed and memory.
- Poor performance and perception of speech.
- Increased tendency to depression, anxiety and irritability.
- A tendency to faster frequencies and higher voltages in EEG.

Extrapyramidal manifestations (dystonia, rest tremors, cogwheel rigidity and chorea-athetosis).[39] may occur four to forty days after organophosphorous poisoning. Recent studies suggest that Parkinson's disease is a more common in patients who report to have had previous exposure to pesticides.[40]

Other effects of organophosphorous intoxication

- **Altered immunity to infection**

In 1974, *Bellin and Chow*[26] suggested that organophosphorous agents might have an effect on the human immune system. *Casali et al*[27] demonstrated that parathion suppressed both the primary IgM and IgG response to sheep erythrocytes in mice. *Newcombe*[28] showed an increased incidence of lymphoproliferative disorders associated with impaired natural killer cell and cytotoxic T-cell function. *Murray et al*[41] reported influenza like symptoms in 23 patients after occupational exposure to organophosphorous compounds.

- **EFFECTS ON CARDIOVASCULAR SYSTEM**

The mechanism by which organophosphates and carbamates induce cardiotoxicity is still uncertain.

Ludomirsky et al[5] described three phases of cardiac toxicity after organophosphate poisoning:

- Phase 1 - a brief period of increased sympathetic tone
- Phase 2 - a prolonged period of parasympathetic activity
- Phase 3 - Q-T prolongation is followed by torsade de pointes, ventricular tachycardia, and then ventricular fibrillation.

Both sympathetic and parasympathetic over-activity have been shown to cause myocardial damage.[6,7]

The cardiac toxicity associated with organophosphate and carbamate poisoning is caused by more than one mechanism. Possible mechanisms include sympathetic and parasympathetic over-activity, hypoxemia, acidosis, electrolyte derangements, and a direct toxic effect of the compounds on the myocardium. Some investigators[5,42] have described a polymorphic ventricular tachycardia of the torsade de pointes type attributed to a prolongation of the Q-Tc interval associated with organophosphate poisoning. Administration of atropine in high doses has been implicated in the development of ventricular arrhythmias.[43,44]

Lyzhnikov et al[42] and *Ludomirshy et al*[5] also found no correlation between atropine therapy and ventricular arrhythmias in organophosphate poisoning. Hypertension and sinus tachycardia, which may be seen in organophosphate and carbamate poisoning, are nicotinic effects, while hypotension and sinus bradycardia are cholinergic manifestations.[41] Some investigators consider the presence of hypertension and sinus tachycardia to be manifestations of severe poisoning.[45]

- **Effects on Reproduction**

There is a report of termination of pregnancy following organophosphorous poisoning during the first trimester.[7] In experimental animals, organophosphorous poisoning during pregnancy causes pre and postnatal death and congenital abnormalities such as vertebral deformities, limb defect, polydactyl and cleft palate.

- **GI effects**

Profuse diarrhea for 2 to 5 days after ingestion of Organophosphorous insecticides has been reported.

- **Blood sugar changes in acute OPC poisoning**

Hyperglycaemia and glycosuria have been reported in op poisoning though ketonuria is absent.[8] In 1971, Namba et al reported that "transient hyperglycemia and glycosuria are found in severe organophosphate poisoning. Absence of acetone bodies differentiates from diabetic coma, except for coma in diabetic patient due to hyperosmolarity from excessive blood glucose.[35] Earlier it was postulated that acetylcholine accumulation at sympathetic ganglia sites leads to "Pheochromocytoma-like" increases in catecholamine secretion with subsequent development of hyperglycemia, glycosuria and metabolic acidosis in severe cases. Hyperglycemia has been associated with more complications in literature.[46]

Mechanism of Blood glucose changes in OPP: Though the changes in blood glucose and amylase are well known, the mechanism is not clear.

Probable mechanisms are:

- These chemicals inhibit cholinesterase allowing accumulation of acetylcholine at cholinergic sites resulting in continuous stimulation of cholinergic fibers leading to marked catecholamine excess which can lead to hyperglycemia.[47]

- However, recent studies suggest that occurrence of pancreatitis may be responsible as hyperamylasemia often accompanies hyperglycemia. Though severe acute pancreatitis is not common, sub clinical pancreatic damage can occur following OP poisoning as shown by Dressel et al in canine experiments. In the experimental study they showed that OPCs cause an increase in intraductal pressure and exocrine pancreas flow rate which results in extravasation of fluids.[48]
- Nicotinic receptors function in brain pathways that increase the release of several pituitary hormones in crediting – vasopressin, adrenocorticotropic hormone and prolactin. In animal experiments changes in diurnal pattern of plasma ACTH has been reported following OPP.[47] Persistent cholinergic stimulation could be causing changes in these hormones and can contribute to hyperglycemia.
- There is also experimental evidence to suggest that hyperglycemia could be as a result of increased breakdown of hepatic glycogen.[49]

➢ **Endocrine changes**

Changes in diurnal pattern of plasma adrenocorticotropic hormone have been reported. Nicotinic receptors also function in brain pathways that increase the release of several pituitary hormones including vasopressin, ACTH and Prolactin. Significant decreases in serum concentration of thyroxine and triiodothyroxine and an increased secretion of thyroid stimulating hormone were observed after OP poisoning. Hyperamylasemia and acute pancreatitis have also been reported

- **Temperature Regulation**

After exposure to most organophosphorous compounds, a marked hypothermia response lasting upto 24 hours has been demonstrated.[42]

DIAGNOSIS

Diagnosis depends on the following factors:

- History or evidence of exposure to anti-cholinesterase agents.
- Signs and symptoms of poisoning.
- Improvement of these clinical features with atropine and PAM.
- Inhibition of cholinesterase activity.

In most patients, a history of exposure to organophosphorous insecticide can be obtained. A container is usually found. History may be denied in attempts of suicide or unavailable in-patients who are found unconscious.

Organophosphates impart a garlic-like odour to the breath, vomitus or faeces.[19] The signs of organophosphorous poisoning that are most helpful in diagnosis are miosis and muscle fasciculations. Others include excessive perspiration, salivation, lacrimation and bronchial secretion.[19,29]

OP poisoning is generally diagnosed clinically based on the characteristic symptoms and the history of exposure to OP agents.[50] When the diagnosis is not evident, a depressed serum or RBC cholinesterase level is helpful (<50%).

Table 5: Estimation of severity of poisoning based on cholinesterase activity[51,52]

Type of poisoning	Estimated cholinesterase activity
Mild	20 - 50%
Moderate	10 - 20%
Severe	< 10%

If OP poisoning is suspected, therapy should never be withheld pending confirmation of laboratory values.[51]

DIAGNOSTIC TESTS

- Atropine challenge - as an adjunct to clinical examination, this is used as a diagnostic aid in patients with suspected OP toxicity.[53] A dose of 1 - 2mg atropine is administered IV and the patients clinical response is observed. Patients with muscarinic effects from other causes should improve significantly after atropine. If no clinical improvement occurs, the patient is considered likely to have OP poisoning.
- Serum, urinary or tissue levels of most OPCs can be performed, provided the offending agent is known or suspected.[54]
- Measurements of Butryl choline esterase and RBC cholinesterase activity serve as proxy markers for neuronal AChE activity and are the most useful methods for confirming OP exposure. They can be assayed on routine blood samples. In general, RBC cholinesterase activity levels are more specific, and correlate better with the severity of clinical effects than BChE levels.[55]

TYPES OF CHOLINESTERASE[45,50,56,57,58]

Two major forms of cholinesterase exist in vertebrates which hydrolyze acetyl choline:

- **Plasma Cholinesterase (pseudo- or Butryl Cholinesterase)**: it is found in plasma, liver, pancreas and intestinal mucosa. (Liver being the main organ). Variations occur due to liver disease, chronic inflammation, malnutrition, morphine, codeine, succinylcholine administration and hypersensitivity reactions.
- **RBC Cholinesterase (true/specific)**: it is found in nervous tissue, erythrocytes, lung, spleen and grey matter. It is decreased in pernicious anemia and after anti-malarial therapy.

Most of the OPCs inhibit both pseudocholinesterase and Ach. Estimation of acetyl-cholinesterase is theoretically preferred, since it would reflect the degree of inhibition of synaptic cholinesterase (acetylcholinesterase). Estimation of butryl cholinesterase has an advantage because the measurement is simpler and more accurate than estimation of the acetylcholinesterase. Butrylcholinesterase indicate the prior presence of cholinesterase inhibition even after recovery of acetylcholinesterase activity by pralidoxime.

In severe poisoning, return to normal requires about 4 weeks for BChE and about 5 weeks for AChE. AChE regenerates at approximately 1% per day whereas enzyme in the plasma regenerates at a more rapid rate, approximately 25% in the first 7 - 10 days. The confirmation of diagnosis depends on demonstrating reduced cholinesterase activity

in the circulatory blood. Activity is expressed as percentage of normality of healthy adults.

Table 6: Interpretation of Cholinesterase[59]

	RBC cholinesterase	Plasma cholinesterase
Advantage	Better reflection of synaptic inhibition	Easier to assay declines faster
Site	CNS gray matter, RBC, motor end plate	CNS white matter, plasma, liver, pancreas, heart
Regeneration (untreated)	1% per day	25-30% in fist 7-10 days
Normalization (untreated)	35-49 day	28-42 days
Use	Unsuspected prior exposure with elevated plasma cholinesterase	Acute exposure
False depression	Pernicious anemias, haemoglobinopathies, antimalarial treatment, oxalate blood tubes.	Liver dysfunction, malnutrition, hypersensitivity reactions, drugs (succinylcholine, codeine, morphine) pregnancy, genetic deficiency

Advantages of estimation of butrylcholinesterase[58,60,61,62]

1. Determination of BChE was advantageous in that it is simpler and more accurate.
2. In acute poisoning, manifestations generally occur after more than 50% of serum cholinesterase is inhibited and the severity of manifestation parallels the degree of serum cholinesterase activity.

3. Following pralidoxime administration, reactivation of serum cholinesterase is slow compared to erythrocyte cholinesterase.
4. Plasma can be refrigerated for a week without appreciable loss of cholinesterase activity.

Disadvantages of estimation of Butrylcholinesterase

1. Normal values are widely variable from person to person, as well as in same individual at different times.
2. Low levels can be attributed to certain clinical states and genetic factors.
3. Following pralidoxime administration, RBC cholinesterase indicates the effectiveness of PAM and serum cholinesterase indicates the prior presence of cholinesterase inhibition even after recovery of RBC cholinesterase activity by PAM. Hence, the latter cannot be used to assess the effectiveness of PAM therapy.
    - Repetitive nerve stimulation is a promising modality for asessing the degree of AChE inhibition at the NMJ both during the acute phase and during IMS.
    - Routine electromyography may also be a helpful adjunct in the evaluation of OP - induced muscle weakness.
    - Arterial blood gas and oximetry measurements are used to assess the adequacy of the patient's ventilation and oxygenation and may help indicate the need for additional antidotal treatment or endotracheal intubation.

- Chest radiography to look for pulmonary edema and to confirm cases of suspected pulmonary aspiration and hydrocarbon pneumonitis.
- ECG should be performed due to the risk of bradyarrhythmias and cardiac conduction defects.
- Liver biochemical abnormalities have been reported and hence monitoring should be done after significant exposure.
- Serum electrolytes and renal function should be assessed in patients with significant secretions and fluid loss.
- Non-specific abnormalities seen are:
  - Leukocytosis
  - Acidosis (hypoventilation or hypotension)
  - Hypokalemia
  - Raised AST and LDH
  - Elevated creatinine kinase

MANAGEMENT

All patients should be managed as emergencies in hospital.

A. Acute Cholinergic Crisis[19]

Treatment is based on the following principles:

- Minimizing further absorption of the insecticide.
- Pharmacologically countering the effects of the poison.
- Maintaining vital functions.

Successful management requires rapid and simultaneous implementation of the above principles.

First aid measures should include:

- Removal of patient from the contaminated environment.
- Removal of contaminated clothes and washing of the skin and eyes.

Respiratory failure is the usual cause of death in the acute phase. Resuscitation and artificial respiration may be required immediately. Mouth-to-mouth respiration should not be attempted.

Cardiac arrhythmias include various degrees of heart block and should be managed accordingly.

Gastric lavage is most effective within 30 minutes of ingestion but is advised also at the time of admission after taking necessary precautions to protect the airway. If the patient is semiconscious/unconscious Ryle's tube aspiration can be done. Activated charcoal may be administered to reduce further absorption from the stomach.

ATROPINE

Treatment with anticholinergic medication is still the mainstay of treatment and should be started as soon as the airway has been secure. Atropine acts as a physiological antidote, effectively antagonizing the muscarinic-receptor-mediated action. It has virtually no effect against the peripheral neuromuscular dysfunction and subsequent paralysis induced by organophosphorous agent. A recommended dose is 2-4 mg intravenous, repeated at interval of 5-10 minutes initially and continued until signs of atropinisation (dry mucous membrane, dilated pupils, flushing of skin and a heart rate of

> 100 beats/minute) appear. Atropine therapy should be maintained until there is complete recovery.

Infusion of atropine is used in some centers in dose of 0.02-0.08 mg/kg/hr.[63] Infusion of atropine has produced significant reduction in mortality in some centers when compared to conventionally intermittent therapy.[64] A heart rate exceeding 140 beats/minute should be avoided. ST-segment abnormalities in the ECG may be induced by large doses of atropine. These may be corrected with *Propronalol,* eliminating any need to reduce the rate of administration of atropine. Atropine crosses the blood brain barrier and may cause severe toxic effects such as convulsions, psychosis and coma.[53]

GLYCOPYRROLATE

This is a quaternary ammonium compound can be used as an alternative to atropine. The advantages of Glycopyrrolate over atropine are:

- Better control of secretions[54]
- Less tachycardia[55]
- Fewer CNS side effects.[56]

OXIMES

The observation that oximes reactivates phosphorylated AchE more rapidly than spontaneous hydrolysis led to the development of Pralidoxime (Pyridine-2-aldoxime methyl chloride, PAM) and later Obidoxime. The reactivating action of Pralidoxime is

most marked at the skeletal neuromuscular junction. It acts by reactivation of the inhibited phosphorylated enzyme to free the active form.

Initial adult dose of 2-PAM Cl is 1.0 g intravenously. Loading dose of 20-50mg/kg based on symptoms severity (dissolved in 0.9% NS infused over 30 minutes), followed by a continuous infusion of 10-20mg/kg/hr. The maximum recommended dose in adults is 12gm in 24 hours.

It has no effect on the muscarinic effect. It has short half-life of 1-2 hours when given intravenously[65] and does not cross the blood brain barrier.[10]

PAM should be administered as early as possible, at least within 4-36 hours as regeneration of AchE. It is dependent primarily on the life span of the erythrocytes when aging of the enzyme has occurred.[21]

PAM is available as Chloride, Iodide, Mesylate and Methyl Sulfate salts. The Chloride salt is more stable than iodide in dry state and is preferred for intramuscular use. The major pharmacological action of oximes is to reactivate AchE by removal of phosphate group bound to the esteritic site.[8] This action occurs shortly after poisoning and inhibition of the enzymes, after which the enzyme ages and becomes more firmly bound to esteratic site.[66] Oximes should be given as soon as possible before aging takes place. They are most effective if given within 6 hours of poisoning, but beneficial response is seen upto 24 hours of poisoning.

The therapeutic effects of oximes seemed to depend on the plasma concentrations of the Organophosphorous agent with the benefit being minimal at high concentrations of Organophosphorous in the blood. Pralidoxime does not cross the blood-brain barrier whereas Obidoxime does. Paradoxically high doses of pralidoxime may cause neuromuscular block and other effects including inhibition of AchE.[10] High frequencies of cardiac arrhythmias were observed in patients who received high cumulative doses of atropine and Obidoxime.

DIAZEPAM

Some reports have indicated that benzodiazepines are useful as antidotes in poisoning by anticholinesterases.[67] This appears to counteract some aspects of CNS derived symptoms and also increase therapeutic effects of atropine and PAM. Diazepam is used to treat convulsions after organophosphorous poisoning and in the support of ventilatory care.

FLUORIDE

Fluoride and atropine combination produces a greater antidote effect than atropine alone.[21] It was noted that increased cholinesterase levels were observed in workers in a plastic factory handling fluoride compounds.

MAGNESIUM

Kiss and Fazekas[68] reported that ventricular premature contractions were successfully eliminated with Intravenous Magnesium Sulfate. The magnesium was thought to counteract direct toxic inhibitory effect of organophosphates on Sodium-Potassium ATPase.

PHENOTHIAZINES

The use of phenothiazines in the management of organophosphorous poisoning is controversial. Diazepam has proved to be satisfactory and popular alternative.[19]

RESPIRATORY STIMULANTS

Respiratory stimulants should not be used in the treatment of organophosphorous poisoning in humans, particularly, in view of the bronchospasm, neuromuscular block and convulsions that are associated with intoxication.[69]

OTHER MEASURES

- Dialysis of blood against activated charcoal (hemoperfusion) is effective in Demeton-S-Methyl Sulphoxide; Dimethoate & Parathion poisoning.[52]
- Prompt improvements have been reported following repeated injections of purified human cholinesterase.[20]
- Sodium bicarbonate is sometimes used for treatment of OP poisoning in Brazil and Iran, in place of oximes. Increases in blood pH (upto 7.45 – 7.55) have been reported to improve outcome in dogs through an unknown mechanism.[70]

- The alpha2-adrenergic receptor agonist clonidine also reduces acetylcholine synthesis and release from presynaptic terminals. Animal studies show benefit of clonidine treatment, especially in combination with atropine, but effects in human beings are unknown.
- Butyrylcholinesterase scavenges OP in plasma, reducing the amount available to inhibit acetylcholinesterase in synapses. It has been cloned and military research now aims to inject soldiers with the enzyme before exposure to OP nerve gases. Such a prophylactic approach is not practical for self-poisoning with OP because we cannot predict when a person is going to ingest the pesticide.
- A better approach than use of butylcholinesterase might be to give recombinant bacterial phosphotriesterases, or hydrolases. These proteins breakdown OP pesticides enzymatically and protect from poisoning. Future clinical development of such enzymes could reduce blood concentrations of OP, allowing optimum activity of other treatments.[71]

  However, all these regimens need further evaluation.[19]

ROLE OF ANTIOXIDANTS IN OP POISONING

The toxicity of OP compounds is mediated by generation of nitric oxide and other free radicals. These toxic molecules can be counteracted by antioxidants such as vitamins C and E, spin traps, melatonin and low molecular weight thiols. The latter compounds can also increase the synthesis of glutathione, which can both ameliorate the OP induced oxidative stress and enhance OP detoxification.[72] OP compounds are soluble in both water and lipid. Some OP compounds are highly soluble in water and can therefore easily contaminate aquatic ecosystems, thereby increasing the exposure risk of aquatic flora and

fauna. Most of OP compounds are highly lipid – soluble agents and are well absorbed from the skin, oral mucous membranes, conjunctiva, gastrointestinal and respiratory tracts.

Vitamin E is also a family of lipid – soluble vitamins, of which α-tocopherol is the most active form and is powerful biological antioxidant. Vitamin E may effectively minimize oxidative stress, lipid peroxidation and toxic effects of reactive oxygen species in biological systems. Selenium appears to function as an anti-mutagenic agent, preventing the malignant transformation of normal cells. These protective effects of selenium (as co-antioxidant) seem to be primarily associated with its presence in the seleno-enzymes, which are known to protect DNA and other cellular components from oxidative damage.[73] Hence, it is suggested to include antioxidants in the prescription of the patients with OP poisoning.

MANAGEMENT OF INTERMEDIATE SYNDROME[19]

Prompt and effective management of respiratory insufficiency is the cornerstone of treatment of Intermediate syndrome. Patients should be observed for early signs of respiratory failure and facilities for ventilatory care should be made available. Frequent blood-gas analyses are useful in monitoring and weaning from ventilatory support. Diazepam in 10 mg intravenous doses may be useful in anxious or restless patients on ventilator.

MANAGEMENT OF DELAYED NEUROPATHY[19]

No specific drug therapy has proved useful. The muscle weakness benefits from regular exercise and physiotherapy.

COMPLICATIONS

Complications resulting from organophosphorous poisoning occur in about 43% of cases with acute intoxication.[31,74]

RESPIRATORY FAILURE

There are various studies in which respiratory failure was the commonest complication encountered following acute organophosphorous poisoning.[72,75] The pathogenesis is multifactorial and related to aspiration of gastric contents, excessive secretions in the airways, pulmonary infections, pneumonia, septicemia and development of ARDS.[76]

Respiratory consequences of muscarinic overstimulation including rhinorrhoea, bronchorrhea, bronchoconstriction and laryngeal spasm may contribute to respiratory failure. These are often combined with nicotinic effects such as respiratory muscle weakness and paralysis (including paralysis of tongue and nasopharynx).

Central depression of respiration occurs following cholinergic overstimulation of synapses in the brain stem and is a prominent cause of hypoxia, respiratory failure and death in the early period of acute organophosphorous poisoning.[77]

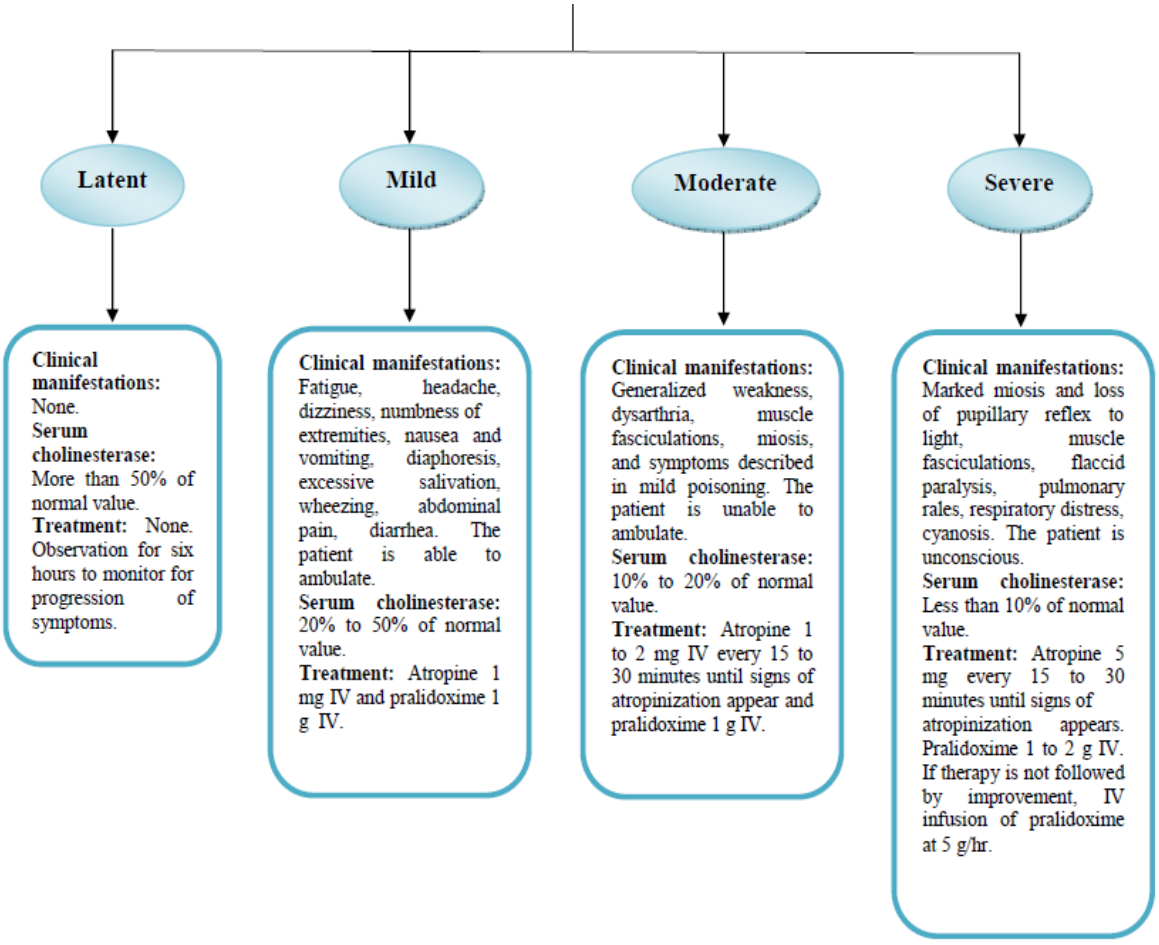
Peripheral neuromuscular block producing respiratory muscle weakness and paralysis as well as the recently described intermediate neuropathy[32] contributes to the development of respiratory insufficiency at a later stage.

Sudden cardiovascular collapse is often the first indication of unsuspected or incipient respiratory failure, a presentation that is associated with a high mortality.[76]

The development of pneumonia is the most important cause of delayed respiratory failure after organophosphorous poisoning and occurs in upto 43% of the patients.[74,76] Upto 80% of patients with pneumonia had respiratory failure; majority of these could be diagnosed within 96 hours of poisoning.[76]

Inadequate or delayed atropinisation appears to be one of the principle reasons for the development of pneumonia[31] and emphasis the importance of skilled medical assessment and treatment at an early stage after poisoning.

Table 7: Summary of Treatment of OPC Poisoning



MORTALITY

Complete recovery usually occurs in 10 days. Mortality rate varies depending on poison used, duration of exposure and atropinisation of all the toxins. In Indian studies, mortality rate ranges between 4-38%. This mortality is similar to other developing countries like Srilanka, and unlike the West where it is < 1%.

Malathion has the lowest toxicity because of rapid hydrolization of carboxyester group to products with little or no anti-cholinesterase activity. Fenthion has the maximum mortality.

DEATH can often occur early (within 24hours) in untreated cases and upto 10 days in hospital with optimal management.[78]

- Early deaths are due to CNS depression, seizures, and ventricular arrhythmias (E.g. Torsade de pointes) or respiratory failure due to excessive bronchial secretions, pulmonary edema, aspiration pneumonia, respiratory muscle paralysis or respiratory center depression.[77]
- Late mortality is caused by respiratory failure[31,76] associated with infections (pneumonia, septicemia) or ventilator related complications.

PREVENTION[7]

Preventive measures should be considered at all the levels of the chain of insecticide movement through the environment-formulation manufacture, mixing application and disposal. Psychiatric counseling for prevention of second episode of poisoning must be done. General counseling and drug therapy for depression. Strict guidelines should be adopted during transport and storage to prevent contamination of food, clothing, drugs, toys, cosmetics and furnishing.

Improved regulation of the availability of pesticides, strict regulation of vendors, and modifications in packaging of pesticides may all help reduce the use of organophosphates as poisons. Adequate provision of information to the public, regular training of health care providers, better availability of drugs/antidotes and the establishment of poison information centres will facilitate in reducing the morbidity and mortality related to organophosphorous poisoning. Insecticides should be kept out of reach of children, to prevent accidental poisoning. During agricultural spraying, proper

precautions should be taken to prevent inhalation and accidental ingestion of the substance.

SCORING SYSTEMS

A number of systems have been proposed for predicting outcome in OP poisoning. The International Program on Chemical Safety (IPCS)/EC/EAPCCT Poison Severity Score (IPCS PSS) was developed by the International Program on Chemical Safety, the European Community, and the European Association of Poisons Centers and Clinical Toxicologists to create a scoring system that produces a qualitative evaluation of the morbidity caused by different forms of poisoning.[70] The utility of the Glasgow coma scale (GCS), the acute physiology and chronic health evaluation (APACHE II) and the Poisoning Severity Score (PSS) in estimating severity and clinical prognosis of OP poisoning has seldom been applied to patients of the Indian subcontinent. Studies are warranted to assess the clinical characteristics, severity, treatment and outcome so as to assist decision makers in choosing the type and extent of therapy required and to find ways to bring down the number of deaths due to self harm. There is a need to assess the usefulness of the GCS, APACHE II, Predicted Mortality Rate and the International Program on Chemical Safety Poison Severity Score (IPCS PSS) to predict death in patients poisoned by OP pesticides.[9] Such survey programs which help in identifying and reporting the exposures and associated health hazards assist in the design of effective preventive and management strategies. Identification of high death risk in patients soon after presentation, allows more intensive monitoring and treatment. A simple system based on clinical features is likely to be most useful in low income countries where the majority of OP poisoning occurs.[78]

GLASGOW COMA SCALE

The Glasgow Coma Scale (GCS) was introduced in 1974 as a method for determining objectively the severity of brain dysfunction and coma six hours after the occurrence of head trauma (HT).[79] Now-a-days, it is by far the most widely used score to assess the severity of HT in clinical research and to compare series of patients.[80] The main advantage of this scale is that it can be utilized by physicians, nurses, and other care providers due to its simplicity.[81]

Standard Glasgow Coma Scale

Eye opening	Best verbal response	Best motor response
4 : spontaneous 3 : to speech 2 : to pain 1 : none	5 : oriented 4 : confused 3 : inappropriate words 2 : incomprehensible sounds 1 : none	6 : obeys commands 5 : localizes 4 : withdraws 3 : abnormal flexion 2 : extension 1 : none
TOTAL GCS SCORE : 3-15		

A score of 13-15, 9-12, 5-8 and 3-4 indicates minor, moderate, severe and very severe injury.[14] Other studies report three GCS score intervals: 13-15 (mild HT), 9-12 (moderate HT) and < 8 (severe HT).[82] Stein et al[83] proposed five intervals: (a) minimal (15, with no LOC or amnesia); (b) mild (14-15 plus amnesia or LOC for 5 minutes or impaired alertness or memory); (c) moderate (9-13 or LOC 5 minutes or focal neurological deficit); (d) severe (5-8); (e) critical (3-4). Many authors suggest that patients with a GCS score of 13 should be included in the moderate HT group, since they present the same risk of complications as patients with a GCS of 9 to 12.[84] It was also stated that alteration in eye and verbal responses scores for more than 1 point and higher

total scores are useful in discriminating between patients with less severe impairment of consciousness.[85,86]

The GCS predicts hospital mortality in ICU patients without trauma[87,88]or with HT[16,80,88,89,]studying 286 non traumatic coma patients found GCS to have the most correct prediction of outcome, Youden index and area under Receiver Operating Characteristic curve as compared to Mainz Emergency Evaluation System (MEES) and APACHE II score. The authors concluded that the GCS score proved to be the best indicator for assessment of mortality thanks to its simplicity, less time-consumption and effectiveness in an emergency department. It was demonstrated that GCS scores were most accurate at outcome prediction when they were combined with age, papillary response and broad outcome categories.[15,90]

POISONING SEVERITY SCORE

A standardized scale for grading the severity of poisoning allows qualitative evaluation of morbidity caused by poisoning, better identification of real risks and comparability of data. The PSS has been published externally.[91] The PSS is a classification scheme for cases of poisoning in adults and children.

This scheme should be used for the classification of acute poisonings regardless of the type and number of agents involved. However, modified schemes may eventually be required for certain poisonings and this scheme may then serve as a model. The PSS should take into account the overall clinical course and be applied according to the most severe symptomatology (including both subjective symptoms and objective signs).

Therefore it is normally a retrospective process, requiring follow-up of cases. If the grading is undertaken at any other time (e.g. on admission) this must be clearly stated when the data are presented. The use of the score is simple. The occurrence of a particular symptom is checked against the chart and the severity grading assigned to a case is determined by the most severe symptom(s) or sign(s) observed. Severity grading should take into account only the observed clinical symptoms and signs and it should not estimate risks or hazards on the basis of parameters such as amounts ingested or serum/plasma concentrations.

The signs and symptoms given in the scheme for each grade serve as examples to assist in grading severity. Treatment measures employed are not graded themselves, but the type of symptomatic and/or supportive treatment applied (e.g. assisted ventilation, inotropic support, hemodialysis for renal failure) may indirectly help in the evaluation of severity. However, preventive use of antidotes should not influence the grading, but should instead be mentioned when the data are presented. Although the scheme is, in principle, intended for grading of acute stages of poisoning, if disabling sequelae and disfigurement occur, they would justify a high severity grade and should be commented on when the data are presented. If a patient's past medical history is considered to influence the severity of poisoning this should also be commented on. Severe cases resulting in death are graded separately in the score to allow a more accurate presentation of data (although it is understood that death is not a grade of severity but an outcome).

Severity Grades

- NONE (0): No symptoms or signs related to poisoning.
- MINOR (1): Mild, transient and spontaneously resolving symptoms.
- MODERATE (2): Pronounced or prolonged symptoms.
- SEVERE (3): Severe or life-threatening symptoms.
- FATAL (4): Death.

APACHE III SCORING SYSTEM

Acute Physiology and Chronic Health Evaluation

The APACHE III mortality estimates are part of a proprietary database and decision support system provided by Apache Medical Systems (McLean, VA). The risk equations and weights were developed by Knaus and colleagues.[92] The APACHE III score is an ICU severity of illness score calculated from the patient's age, the presence of comorbid conditions, and the worst physiologic and laboratory investigations in the first 24 h. The APACHE III risk estimate equations use the admission diagnosis, the source of admission, and the APACHE III score weighted according to coefficients that are not in the public domain.

The performance of the APACHE III first-day predictions have been evaluated on the developmental database.[92] Independent APACHE III validation series are available from Brazil[93], the United Kingdom[94,95] and Germany.[96] In each study, hospital mortality was higher than predicted with resultant poor model calibration. In contrast, in two large, prospective, multicenter North American series[97,98] the APACHE III model demonstrated good overall performance.

METHODOLOGY

SOURCE OF DATA: The study was carried out among 60 consecutive patients of acute organophosphorous compound poisoning who present to the Emergency Department of R. L. Jalappa Hospital, Tamaka, Kolar, and were subsequently admitted under the Department of Medicine.

STUDY DESIGN: Hospital based prospective study.

STUDY PERIOD: 12 months from 1st February 2011 to 31st January 2012.

INCLUSION CRITERIA

- Patients with organophosphorous compound poisoning admitted within 24 hours of consumption of the compound.
- Adult patients with age more than 18 years.

EXCLUSION CRITERIA

- Organo-chlorine and organocarbamate poisonings or unknown compound poisonings
- Patients who were treated at an outside hospital previous to admission.
- Patients who have consumed a combination of different groups of poisons, other poisons and / or drugs.

DIAGNOSIS: A provisional diagnosis of OP poisoning was made on the basis of definite history of OP poisoning by the patient or attendants, and this was substantiated by examination of the container when available. The diagnosis was further substantiated by typical clinical features (miosis, hypersalivation, fasciculation) and characteristic odour of stomach wash or vomitus.

METHODOLOGY: Each patient enrolled for study underwent a detailed clinical examination as per the proforma, specially designed for the study, which included examination for presence of respiratory failure, detailed assessment of CNS and cardiovascular examination.

All patients were given stomach wash and body wash. Intravenous atropine 2-4mg bolus and repeated every 5-15minutes initially until atropinization. The end point of treatment was taken as the drying up of secretions. The atropinization was maintained for 24-48 hours with intermittent doses, every 15-30 minutes or depending on the need, and then tapered over days depending upon patient's response. Pralidoxime chloride was given to all patients as 2g IV bolus over 10-15minutes immediately after admission and 0.5g-1.0g IV 6th hourly for 48hours depending on patient's condition.

Patients were kept under strict observation during their stay in hospital. Assessment of patient's airway and need for endotracheal intubation was assessed. Patients with respiratory failure were intubated and mechanical ventilator support was given.

Psychiatric counseling was done for the patients who survived. Autopsy was conducted on all patients who expire.

INVESTIGATION

All patients underwent following biochemical investigations -

- Routine Haemogram and urine analysis,
- Renal & Liver function Tests,
- Arterial Blood Gas Analysis on admission
- Random Blood Sugar on admission
- Chest X ray
- Serum Electrolytes
- Serum pseudocholinesterase levels on days 1,3,5 and 7
- Electrocardiography
- CPK levels
- Serum amylase levels
- Troponin T levels

METHOD OF ESTIMATION OF PSEUDOCHOLINESTERASE

Pseudocholinesterase was estimated with S-butyryl thiocholine iodide using Dibucaine as inhibitor. Cholinesterase catalyses the hydrolysis of S-butyrylthiocholine Iodide to thiocholine iodide and butyrate. Thiocholine iodide reacts with 5.5 – dithiobis – 2 – nitrobenzoate (DTNB) and forms the yellow coloured product 5-mercapto – 2 - nitrobenzoate. The substrate specificity prevents interference with cholinesterase liberated from erythrocytes even during slight hemolysis. The rate of formation of

6 mercapto – 2 – nitro benzoate is directly proportional to the catalytic cholinesterase activity. It is determined by measuring the increase in absorbance at 480 nm. Normal values of serum pseudocholinesterase ranges from 4150 to 7200 U/L.

Ethical committee clearance was obtained before commencing the study.

STATISTICAL METHODS[99,100,101,102]

Descriptive statistical analysis has been carried out in the present study. Results on continuous measurements are presented on Mean±SD (Min-Max) and results on categorical measurements are presented in Number (%). Significance is assessed at 5% level of significance.

Student "t" test (two tailed, independent) has been used to find the significance of study parameters on continuous scale between two groups Inter group analysis) on metric parameters. Leven1s test for homogeneity of variance has been performed to assess the homogeneity of variance. Chi-square/Fisher Exact test has been used to find the significance of study parameters on categorical scale between two or more groups.

1. SAMPLE SIZE ESTIMATION

Proportion Known populations

$n = [(z^2 * p * q) + ME^2] / [ME^2 + z^2 * p * q / N]$

Proportion Unknown population

$n = [(z^2 * p * q) + ME^2] / (ME^2)$

ME: is the margin of error, measure of precision and Z is 1.96 as critical value at 95%CI

N: population size

n: Sample size

σ: Standard deviation

z: Critical value based on Normal distribution at 95% Confidence Interval

Standard deviation: $SD = \sqrt{\frac{\sum (x - \bar{x})^2}{n-1}}$

2. CHI-SQUARE TEST

The chi-square test for independence is used to determine the relationship between two variables of a sample. In this context independence means that the two factors are not related. In the chi-square test for independence the degree of freedom is equal to the number of columns in the table minus one multiplied by the number of rows in the table minus one

$\chi^2 = \frac{\sum (Oi - Ei)^2}{Ei}$, Where Oi is Observed frequency and Ei is Expected frequency

With (n-1) df

The Assumptions of Chi-square test

The chi-square test, when used with the standard approximation that a chi-square distribution is applicable, has the following assumptions:

- **Random sample**: A random sampling of the data from a fixed distribution or population.

- **Sample size (whole table)**: A sample with a sufficiently large size is assumed. If a chi square test is conducted on a sample with a smaller size, then the chi square test will yield an inaccurate inference. The researcher, by using chi square test on small samples, might end up committing a Type II error.
- **Expected Cell Count**: Adequate expected cell counts. Some require 5 or more, and others require 10 or more. A common rule is 5 or more in all cells of a 2-by-2 table, and 5 or more in 80% of cells in larger tables, but no cells with zero expected count. When this assumption is not met, Fisher Exact test or Yates' correction is applied.

3. FISHER EXACT TEST

The Fisher Exact Test looks at a contingency table which displays how different treatments have produced different outcomes. Its null hypothesis is that treatments do not affect outcomes-- that the two are independent. Reject the null hypothesis (i.e., conclude treatment affects outcome) if *p* is "small".

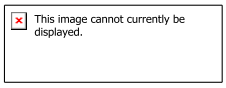
The usual approach to contingency tables is to apply the χ^2 statistic to each cell of the table. One should probably use the χ^2 approach, unless you have a special reason. The most common reason to avoid χ^2 is because you have small expectation values

	Class 1	**Class 2**	**Total**
Sample 1	A	B	a+b
Sample 2	C	D	c+d
Total	a+c	b+d	n

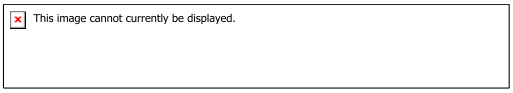
2x2 Fisher Exact Test statistic= $$\sum p = \frac{(a+b)!(c+d)!(a+c)!(b+d)!}{n!}\frac{1}{\sum a!b!c!d!}$$

Fisher Exact test (rxc tables)

Let there exist two such variables X and Y, with m and observed states, respectively. Now form an matrix in which the entries represent the number of observations in which and . Calculate the row and column sums and , respectively, and the total sum



of the matrix. Then calculate the conditional probability of getting the actual matrix given the particular row and column sums, given by



which is a multivariate generalization of the hypergeometric probability function.

4. STUDENT "t" TEST (TWO TAILED, INDEPENDENT)

Assumptions: Subjects are randomly assigned to one of two groups. The distribution of the means being compared are normal with equal variances.

Test: The hypotheses for the comparison of two independent groups are:

H_o: $u_1 = u_2$ (means of the two groups are equal)

H_a: u_1 u_2 (means of the two group are not equal)

The test statistic for is t, with $n_1 + n_2 - 2$ degrees of freedom, where n_1 and n_2 are the sample sizes for groups 1 and 2. A low p-value for this test (less than 0.05 for example) means that there is evidence to reject the null hypothesis in favor of the alternative hypothesis. Or, there is evidence that the difference in the two means are statistically significant. The test statistic is as follows

t-Test: Two-Sample Assuming Equal Variances

$$S_P = \sqrt{\frac{(n_1 - 1)S_1^2 + (n_2 - 1)S_2^2}{n_1 + n_2 - 2}}$$

In all work with two-sample t-test the degrees of freedom or df is:

$$df = n_1 + n_2 - 2$$

The formula for the two sample t-test is:

$$T = \frac{\overline{X} - \overline{Y}}{S_p \sqrt{\frac{1}{n_1} + \frac{1}{n_2}}}$$

Pre-test: Test for variance assumption: A test of the equality of variance is used to test the assumption of equal variances. The test statistic is F with n_1-1 and n_2-1 degrees of freedom.

t-Test: Two-Sample Assuming Unequal Variances

$$T = \frac{\overline{X} - \overline{Y}}{\sqrt{\frac{S_X^2}{n_1} + \frac{S_Y^2}{n_2}}}$$

Note in this case the Degree of Freedom is measured by

$$df' = \frac{\left(\frac{s_1^2}{n_1} + \frac{s_2^2}{n_2}\right)^2}{\frac{\left(\frac{s_1^2}{n_1}\right)^2}{n_1 - 1} + \frac{\left(\frac{s_2^2}{n_2}\right)^2}{n_2 - 1}}$$

and round up to integer.

Results of the t-test: If the p-value associated with the t-test is small (< 0.05), there is evidence to reject the null hypothesis in favor of the alternative. In other words, there is evidence that the means are significantly different at the significance level reported by the p-value. If the p-value associated with the t-test is not small (> 0.05), there is not enough evidence to reject the null hypothesis, and you conclude that there is evidence that the means are not different.

5. SIGNIFICANT FIGURES

+	Suggestive significance	(p value: $0.05<p<0.10$)
*	Moderately significant	(p value: $0.01<p\leq 0.05$)
**	Strongly significant	(p value: $p\leq 0.01$)

Statistical software: The Statistical software namely SAS 9.2, SPSS 15.0, Stata 10.1, MedCalc 9.0.1, Systat 12.0 and R environment ver.2.11.1 were used for the analysis of the data and Microsoft word and Excel have been used to generate graphs, tables etc.

RESULTS

292 adult patients with OPC poisoning presented to our emergency with acute intoxication. 80% were mixed poisonings and were hence excluded from the study. An observational clinical study with 60 patients with pure organophosphorous compound intoxication was undertaken. 5 patients were lost to follow up during the course of the study and were hence excluded.

The results of 55 patients included in the study are presented below:

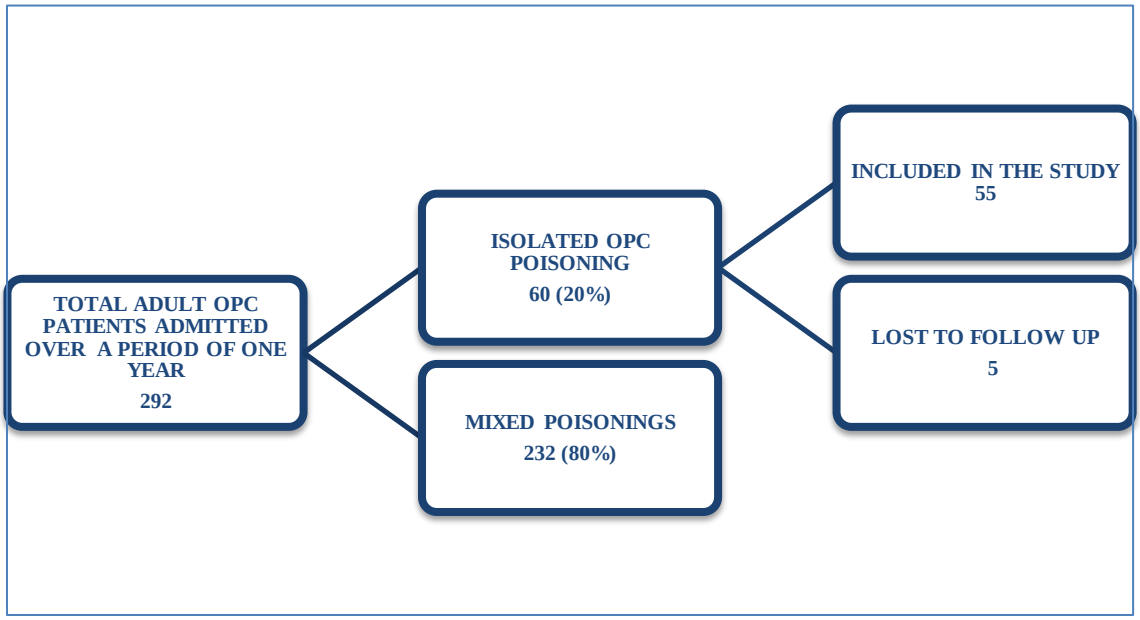
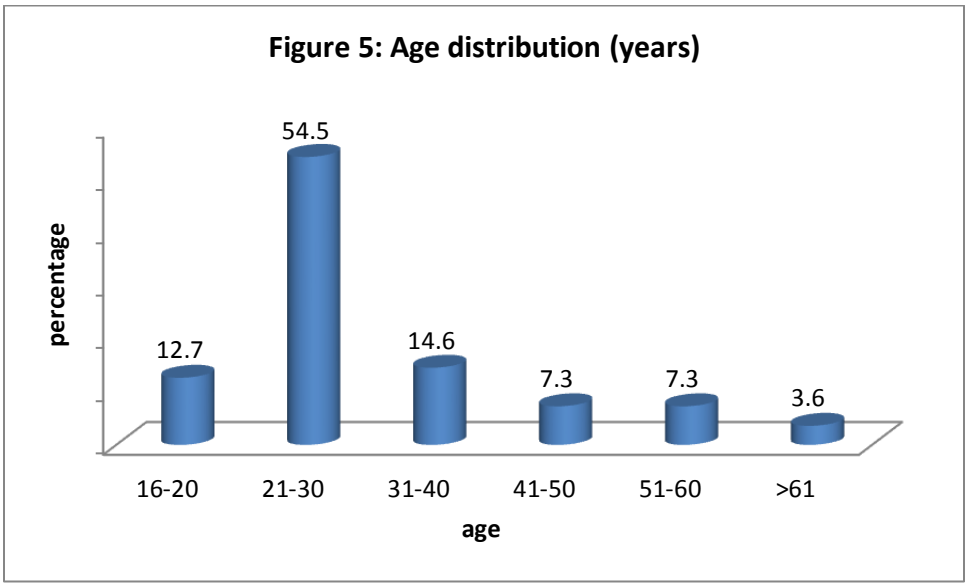


TABLE 8: AGE DISTRIBUTION OF PATIENTS STUDIED

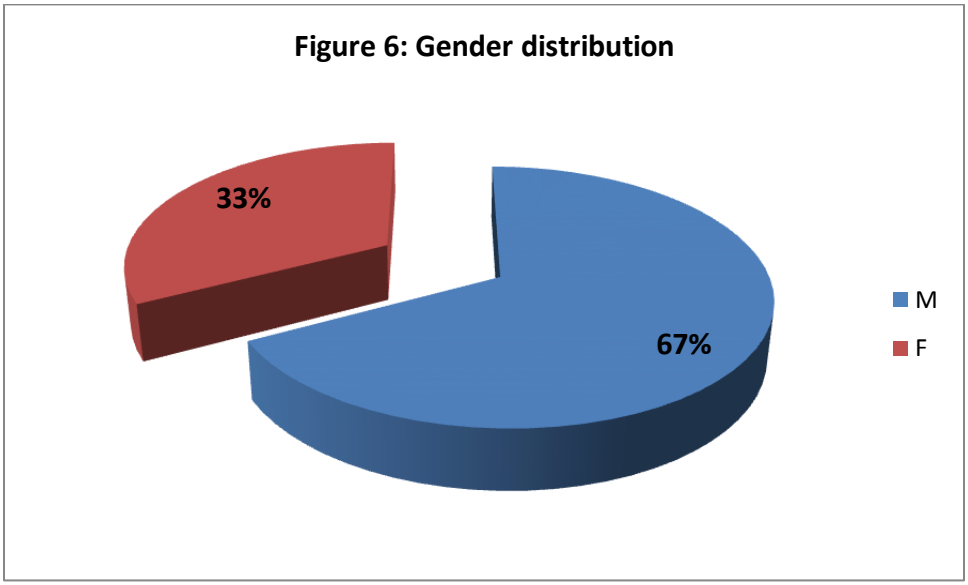
Age in years	Number of patients	%
16-20	7	12.7
21-30	30	54.5
31-40	8	14.6
41-50	4	7.3
51-60	4	7.3
>61	2	3.6
Total	55	100



The youngest person was found to be of 16 years age and the oldest 65 years. The average age at presentation was found to be 28.33 years. 54.5% of the patients were in the 21-30 age group. Only 2 patients were found to be more than 61 years of age. There was an equal number of cases in the 41-50 and 51-60 range, which was 7.3%.

TABLE 9: GENDER DISTRIBUTION OF PATIENTS STUDIED

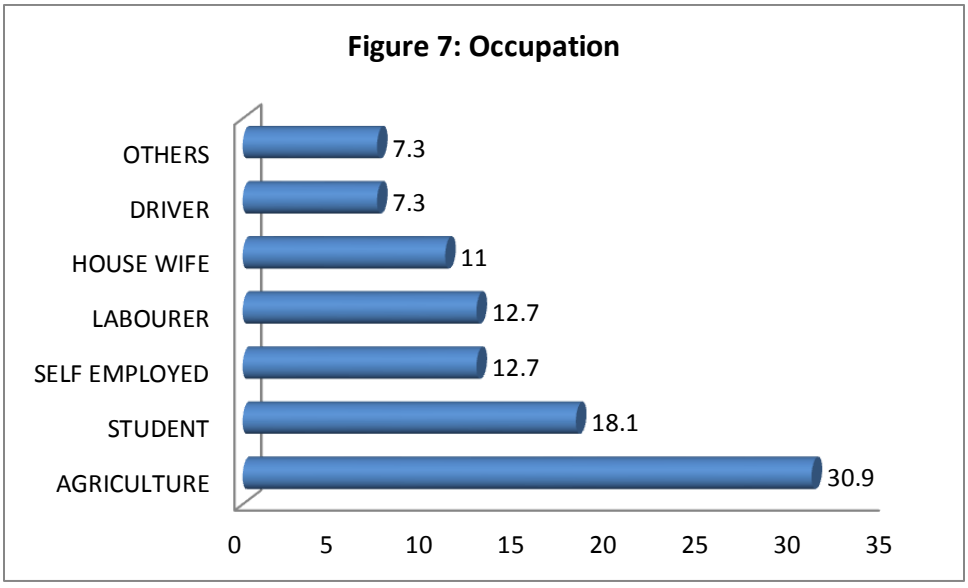
Gender	Number of patients	%
Male	37	67.3
Female	18	32.7
Total	55	100



67.3% of the patients were males and 32.7% were females and the male to female ratio was 2.1:1. Majority of the patients in the study were found to be males.

TABLE 10: OCCUPATION OF THE PATIENT

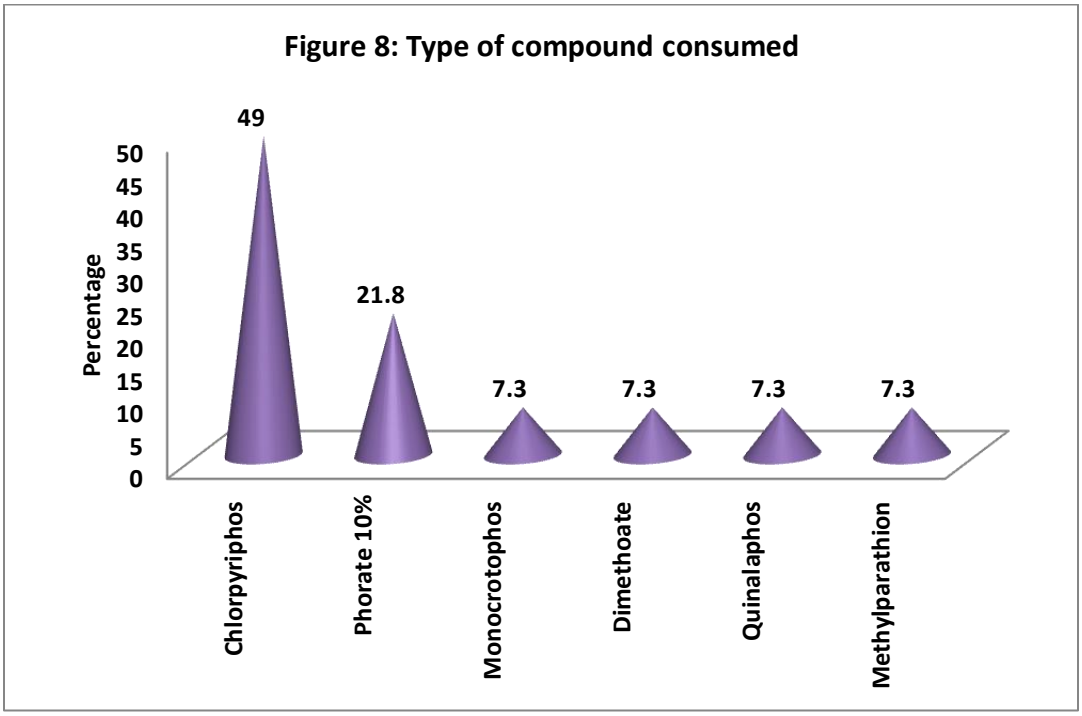
Occupation	Number of patients	%
Agriculture	17	30.9
Student	10	18.1
Self employed	7	12.7
Labourer	7	12.7
House wife	6	11.0
Driver	4	7.3
Others	4	7.3
Total	55	100



The majority of the patients were agriculturists and next were the students. The 4 patients in the others category were one each of businessman, government employee, sericulture and unemployed respectively.

TABLE 11: TYPE OF COMPOUND CONSUMED

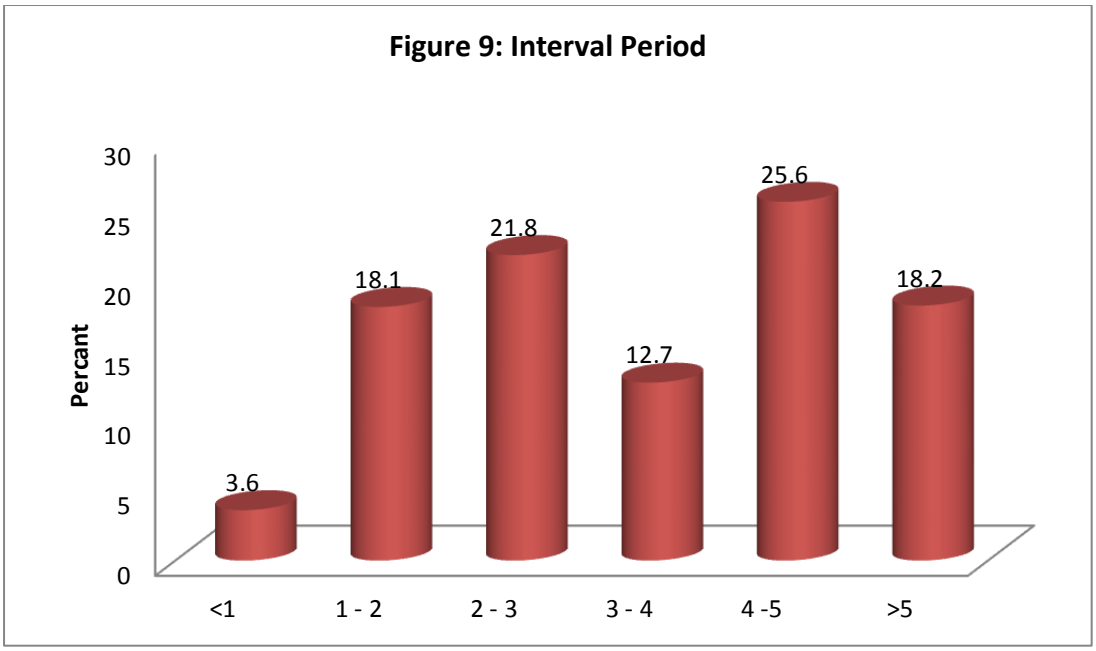
OP compound	Number of patients	%
1.Chlorpyriphos	27	49
2.Phorate 10%	12	21.8
3.Monocrotophos	4	7.3
4.Dimethoate	4	7.3
5.Quinalaphos	4	7.3
6.Methylparathion	4	7.3
Total	55	100



The most common organophosphorous compound consumed was Chlorpyriphos (49%, n = 27) and the least common compounds consumed were Monocrotophos, Dimethoate, Quinalaphos and Methyl Parathion. Phorate was consumed by 12 patients, i.e., 21.8%.

TABLE 12: INTERVAL PERIOD PRIOR TO ADMISSION

Interval Period (hours)	Number of patients	%
<1	2	3.6
1-2	10	18.1
2-3	12	21.8
3-4	7	12.7
4-5	14	25.6
>5	10	18.2
Total	55	100.0



14 patients (25.6%) presented between 4-5 hours after consumption of the compound. The only 2 patients (3.6%) presented within 1 hour of consumption.

TABLE 13: QUANTITY CONSUMED

Quantity (ml)	Number of patients	%
<50 ml	31	56.4
50-100 ml	3	5.4
100 ml	21	38.2
Total	55	100

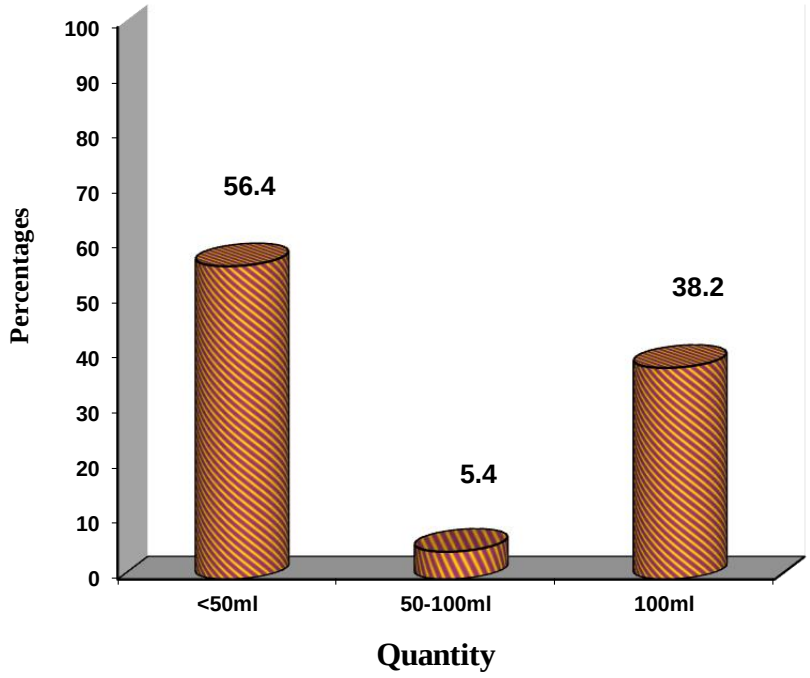


Figure 10: Quantity (ml) used

The quantity ingested by the patient was enquired into either at admission or in case the patient was obtunded, after recovery. Most of the cases (56.4%) consumed less than 50 ml of the compound. 38.2% consumed more than 100 ml and only 3 patients confessed to have consumed between 50 – 100 ml.

TABLE 14: MANNER OF INGESTION OF COMPOUND

Ingested with	Number of patients	%
Alone	43	78.2
With alcohol	7	12.7
With water	5	9.1
Total	55	100

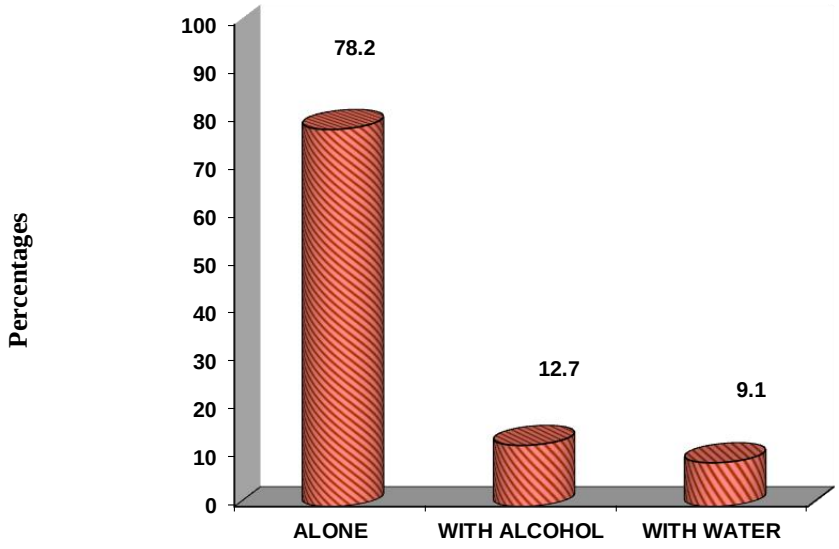


Figure 11: Manner of ingestion of Compound

78% of the patients consumed the poison alone. 13% consumed it with alcohol and about 9% consumed it with water.

TABLE 15: ALCOHOLISM

Alcohol	Number of patients	%
No	45	81.8
Yes	10	18.2
Total	55	100

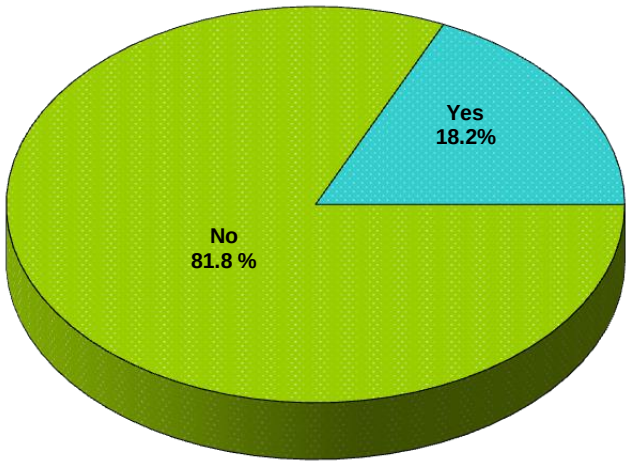


Figure 12: Alcohol intake

18% of the patients were prior alcoholics. Although only 7 of them consumed the compound along with alcohol.

TABLE 16: CHOLINERGIC SYMPTOMS AT PRESENTATION

Cholinergic symptoms	Number of patients	%
No	15	27.3
Yes	40	72.7
Total	55	100

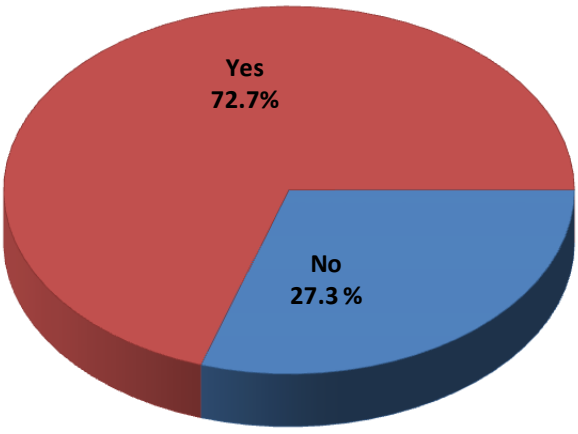


Figure 13: Cholinergic symptoms

Approximately 73% of the patients had cholinergic symptoms (like miosis, lacrimation, salivation, bronchorrhea, diaphoresis) at the time of admission and 27% did not manifest any cholinergic symptoms at presentation.

TABLE 17: GCS SCORE OF PATIENTS STUDIED AT PRESENTATION

GCS	Number of Patients	%
<8	5	9.1
9-12	9	16.4
13-15	41	74.5
Total	55	100

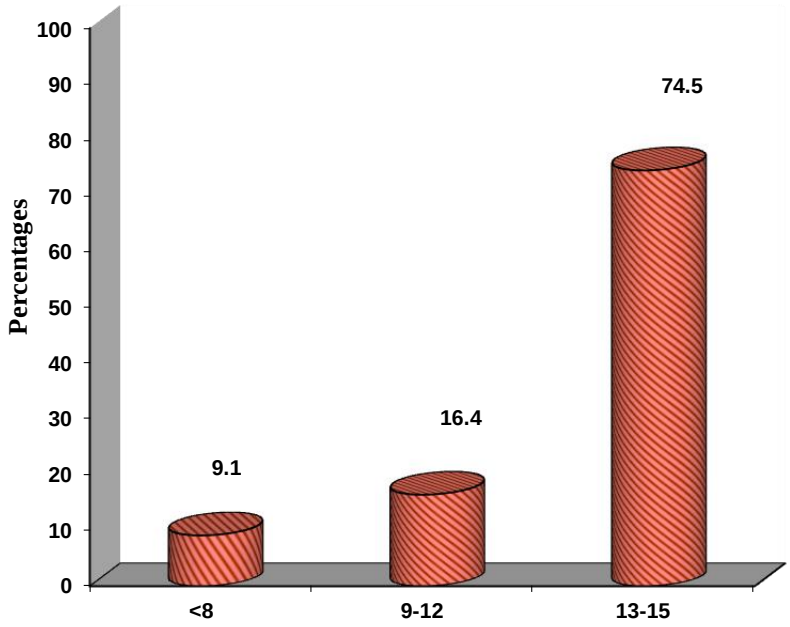


Figure 14: GCS

Approximately 75% of the patients had a GCS between 13-15 at presentation. 16% presented with GCS between 9-12 and 9% of the cases had a GCS less than 8. The average GCS at presentation was 13.

TABLE 18: PSS SCORE AT PRESENTATION

PSS	NUMBER OF PATIENTS	%
None	2	3.6
Minor	26	47.3
Moderate	23	41.8
Severe	4	7.3
Total	55	100

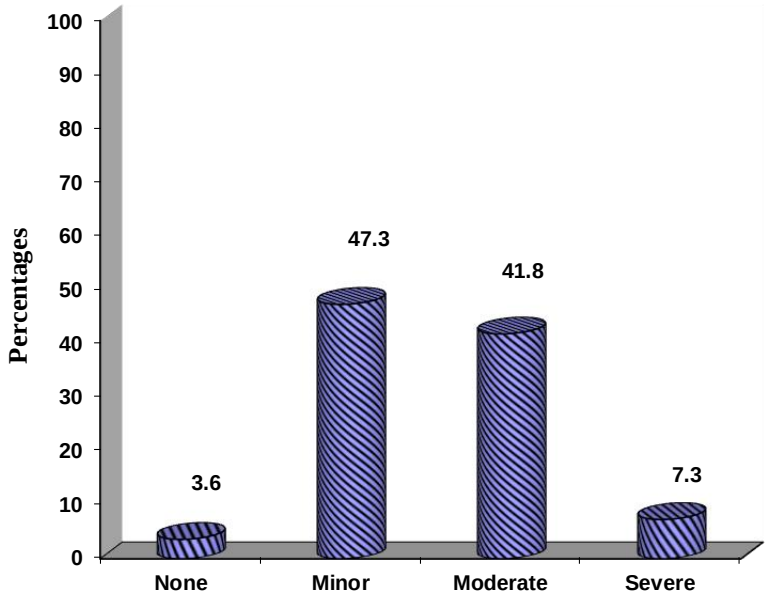


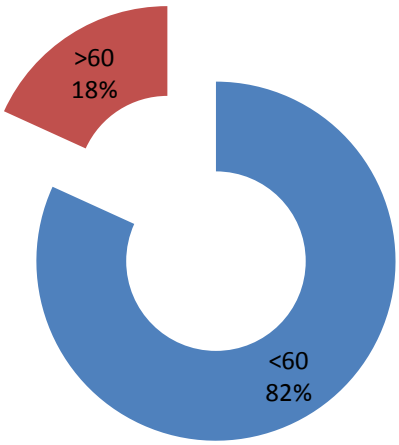
Figure 15: PSS

According to the clinical presentation and the laboratory investigations obtained within first 24 hours of admission, the patients were grouped into Poisoning Severity Score of None, Mild, Moderate, Severe. None of the patients died within the first 24 hours. 47.3% of the cases were found to have mild poisoning, 41.8% had moderate and 7.3% had severe poisoning. Only 2 patients had a score of 0 or none.

TABLE 19: APACHE SCORE AT PRESENTATION

Apache score	Number of patients	%
Less than 60	45	81.8
More than 60	10	18.2
Total	55	100

Figure 16: APACHE III



An APACHE score of less than 60 was taken as normal. The average APACHE score was 43.81. 81.8% of the patients had a score of less than 60 and 18.2 % of the patients had a score more than 60.

TABLE 20: RANDOM BLOOD SUGAR (RBS) LEVELS ON ADMISSION

RBS	Number of patients	%
<75	10	18.2
75-140	31	56.4
>140	14	25.4
Total	55	100

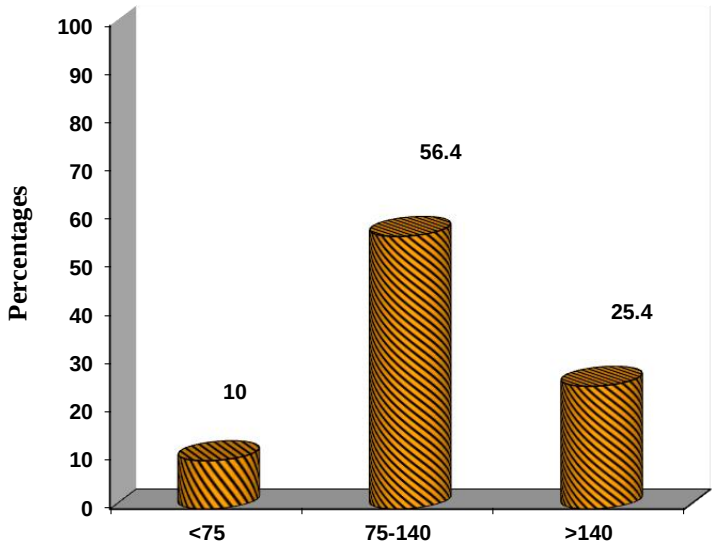


Figure 17: RBS levels on admission

The random blood sugar levels on admission were determined. RBS of less than 75 was considered as hypoglycemia and a sugar reading of > 140 was taken as hyperglycemia. A glucometer reading of less than 75 was noted in 10 patients (18.2%). Majority of the patients had a RBS between 75 and 140. 25.4% had sugar level of more than 140 mg/dl.

TABLE 21: SERUM AMYLASE LEVELS ON ADMISSION

S amylase	Number of patients	%
<130	46	83.6
>130	9	16.4
Total	55	100

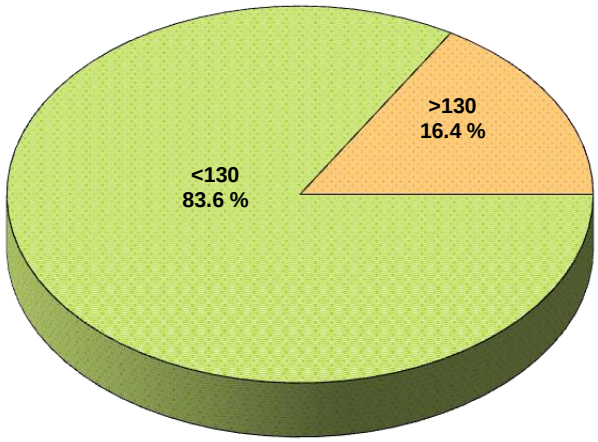
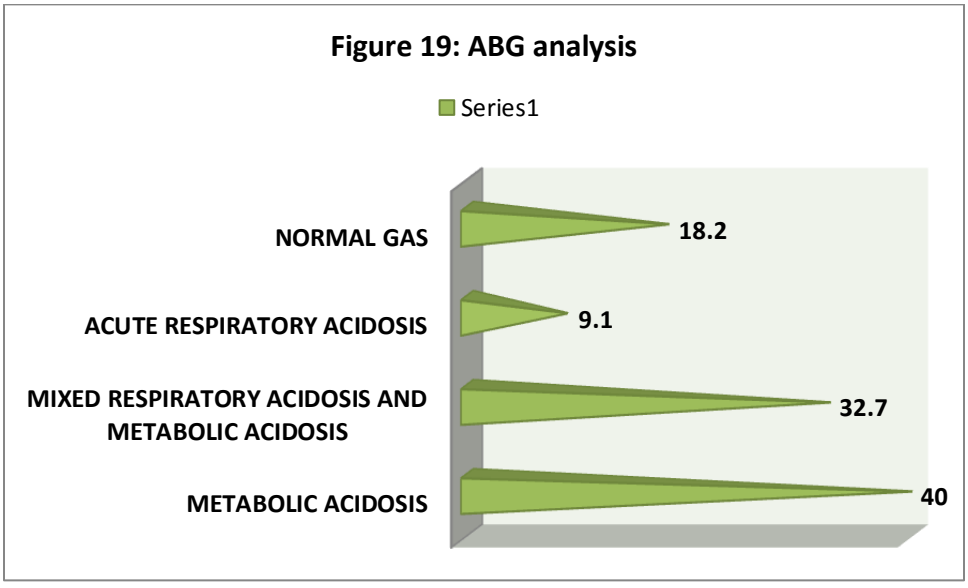


Figure 18: S amlyse on admission

The normal serum amylase levels are less than 130 U/L. 83.6% of the patients had an amylase level less than 130 U/L. 16.4% of the patients had amylase levels of more than 130 U/L.

TABLE 22: ARTERIAL BLOOD GAS ANALYSIS AT PRESENTATION

ABG	Number of patients	%
1.Metabolic acidosis	22	40
2.Mixed respiratory acidosis and metabolic acidosis	18	32.7
3.Acute respiratory acidosis	5	9.1
4.Normal gas	10	18.2
Total	55	100



The most common blood gas pattern on admission was metabolic acidosis. 32.7% of the patients had mixed respiratory and metabolic acidosis; 18.2% had a normal blood gas analysis; 9.1% had acute respiratory acidosis.

TABLE 23: SERUM CPK LEVELS ON ADMISSION

CPK	Number of patients	%
<195	27	49.1
>195	28	50.9
Total	55	100

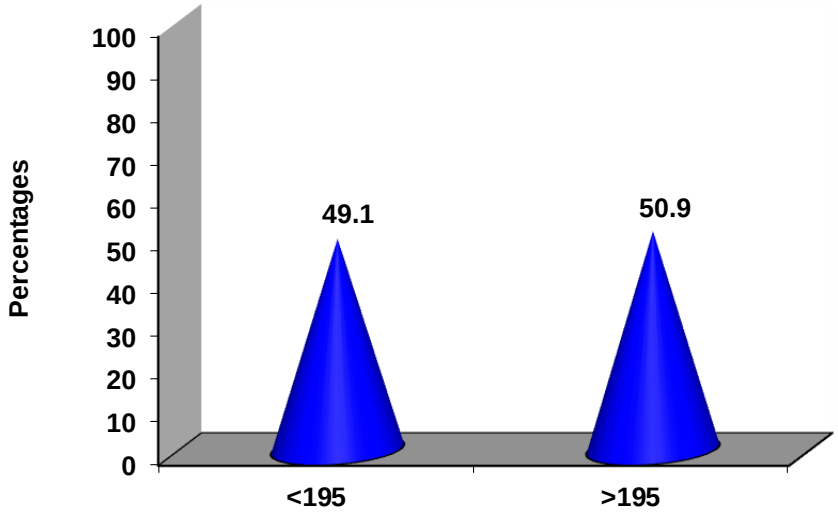
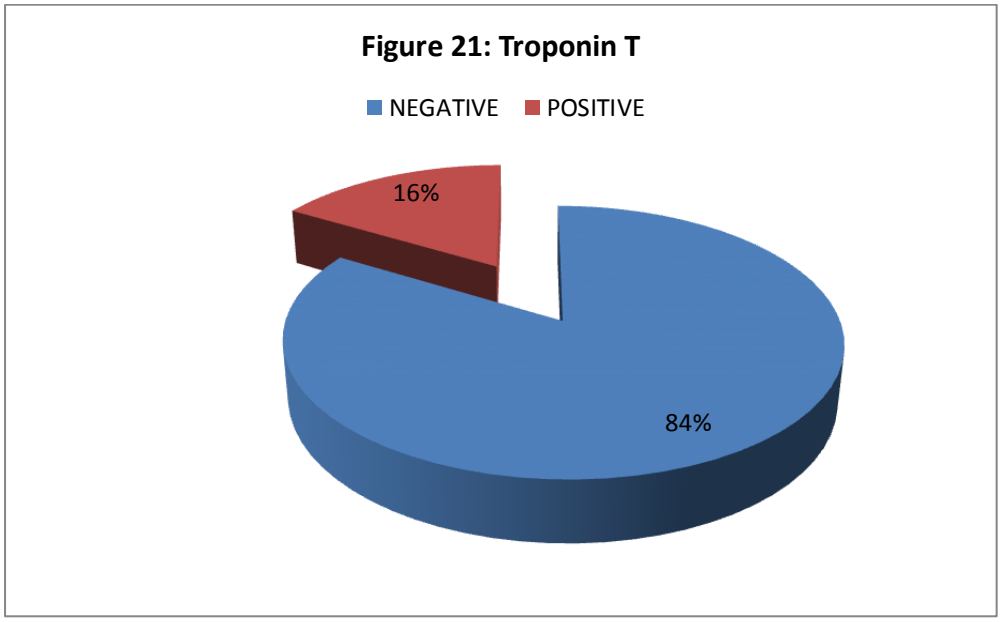


Figure 20: CPK

A CPK level of < 195 is considered to be normal. The serum creatinine Phosphokinase (CPK) levels were more or less equal in both the groups. Almost equal number of patients had normal and elevated levels of CPK.

TABLE 24: TROPONIN T ASSAY ON ADMISSION

TROPONIN T	Number of Patients	%
Negative	46	83.6
Positive	9	16.4
Total	55	100



16.4% of the patients were found to have a positive Troponin T on admission.

Table 25: CKMB LEVEL AT ADMISSION

CKMB	Number of Patients	%
<24	17	31
>25	38	69
Total	55	100

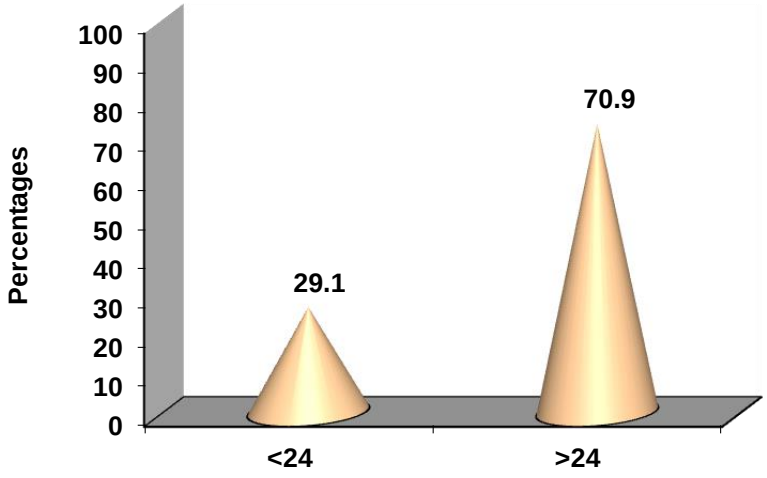


Figure 22: CKMB

69% had an elevated CKMB on admission and 31% had normal values on admission.

TABLE 26: ELECTROCARDIOGRAM ON ADMISSION

ECG	Number of Patients	%
Normal sinus rhythm	35	63.6
Sinus tachycardia	18	32.8
Bundle branch blocks	1	1.8
Extra systole	1	1.8
Total	55	100

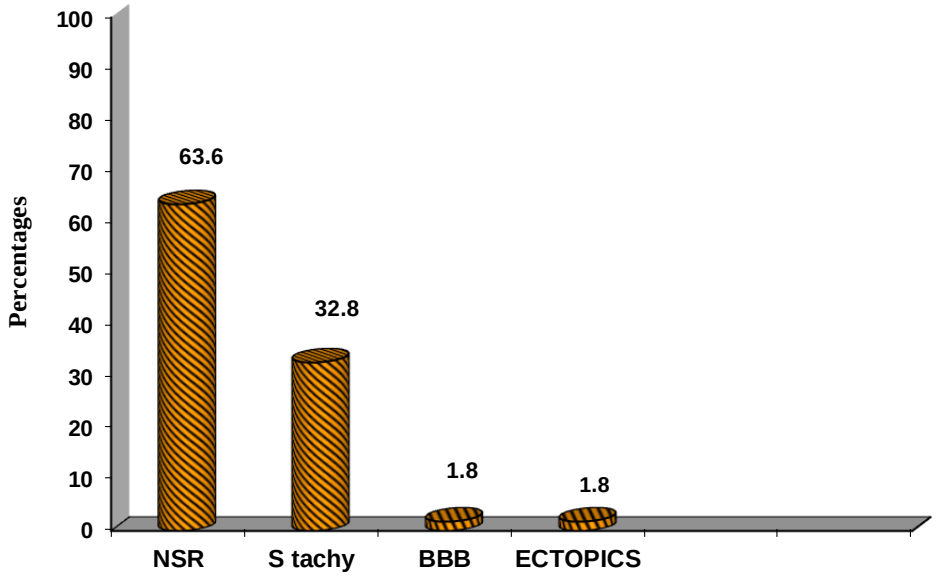


Figure 23: ECG

63.6% of the patients had normal sinus rhythm on admission; 32.8% had sinus tachycardia; 1.8% had bundle branch blocks and extra systole each.

TABLE 27: SERUM PSEUDOCHOLINESTERASE EVALUATION

PCHE	Day 1		Day 3		Day 5		Day 7	
	No.	%	No.	%	No.	%	No.	%
<1000	32	58.2	27	49.1	20	36.4	14	26.9
1000-3000	12	21.8	17	30.9	18	32.7	13	25
>3000	11	20	11	20	17	30.9	25	48.1
Total	55	100	55	100	55	100	52	100
Not available	-	-	-	-	-	-	3	-

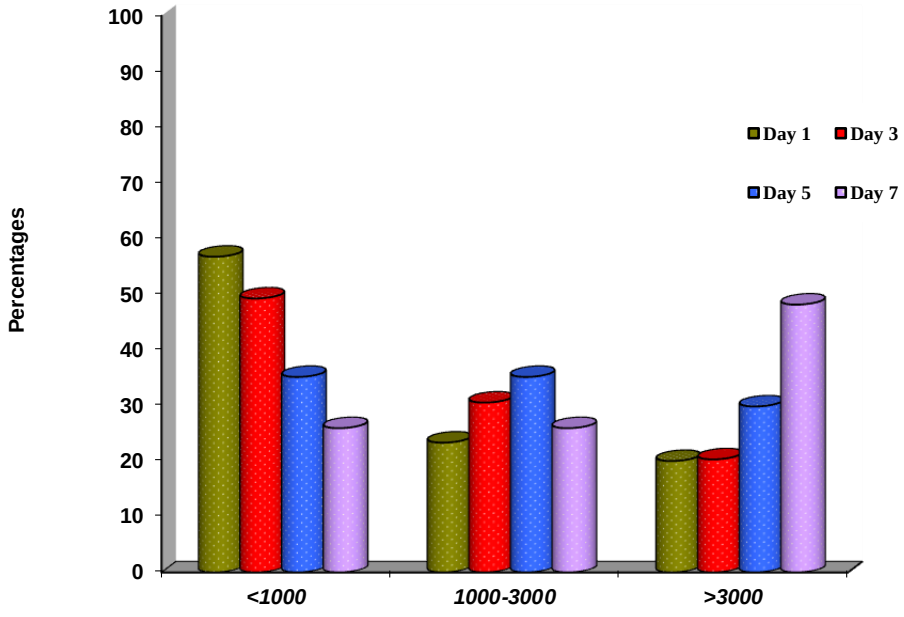


Figure 24: PCHE

The pseudocholinesterase levels were estimated on days 1, 3, 5 and 7 of admission. 58% of the patients had a pseudocholinesterase level of less than 1000 on admission. Of these 49% continued to have low levels on day 3; 36% on day 5 and approximately 27% had persistently low levels on day 7. 20% of the patients had normal levels on admission and continued to have normal levels on day 3. The percentage increased to 31% on day 5 and 48% by day 7.

TABLE 28: SERUM PSEUDOCHOLINESTERASE EVALUATION

Variables	Day 1	Day 3	Day 5	Day 7
Minimum-Maximum	128-13000	200-11000	200-10923	200-8776
Mean ± SD	1844.07±2431.34	1880.49±2233.87	2328.07±2244.83	3216.13±2474.51
p value from day1	-	0.677	0.003	<0.001

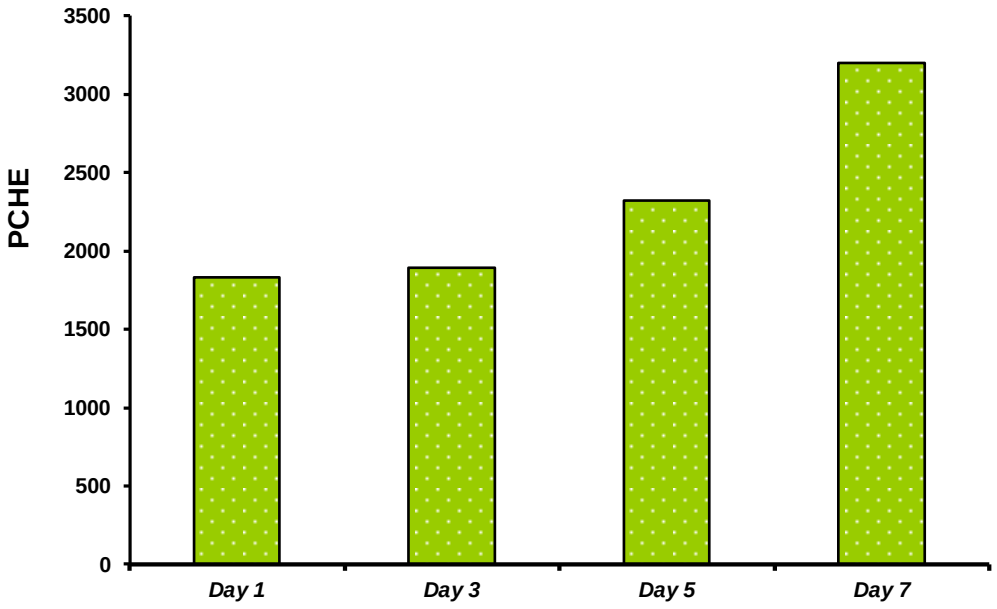


Figure 25: Serum Pseudocholinesterase Evaluation

The average Serum Pseudocholinesterase level on admission (day 1) was 1844 with the least being 128 and the maximum being 13000. On days 3, 5 and 7 the minimum value of pseudocholinesterase found was 200. The maximum level was 8776 on day 7 with the average being 3216 on day 7.

TABLE 29: TOTAL DURATION OF ATROPINE ADMINISTRATION

Atropine duration (days)	Number of patients	%
3 - 5	15	27.3
6 - 9	36	65.4
>10	4	7.3
Total	55	100

Mean ± SD: 5.78 ± 2.21

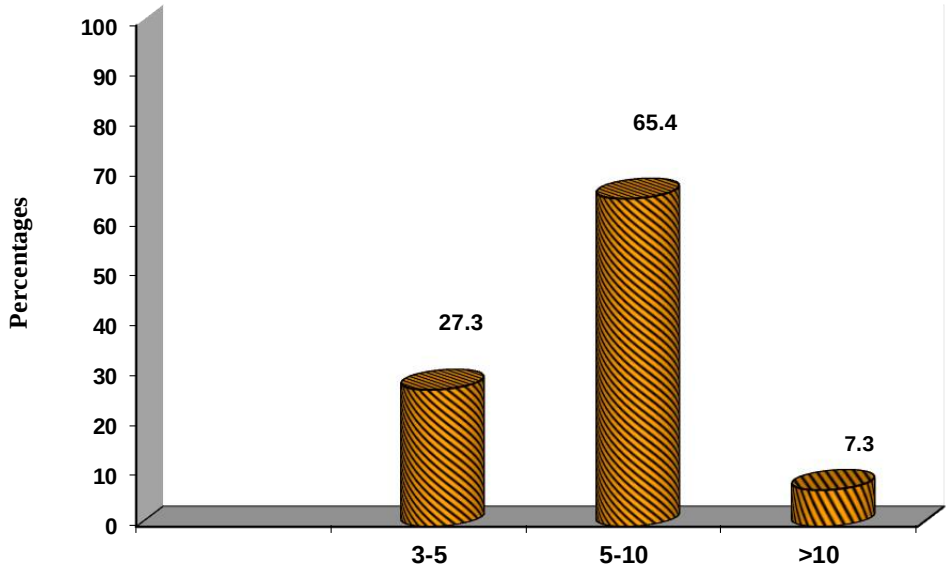


Figure 26: Atropine Duration

Majority of the patients i.e., 65% received atropine infusions between 6 – 9 days. Only 7% received infusions for more than 10 days. The least duration of atropine administered was 3 days and the maximum duration was 13 days. The mean duration of atropine administration was around 6 days.

TABLE 30: NUMBER OF PATIENTS REQUIRING VENTILATORY SUPPORT

Intubated	Number of patients	%
No	44	80
Yes	11	20
Total	55	100

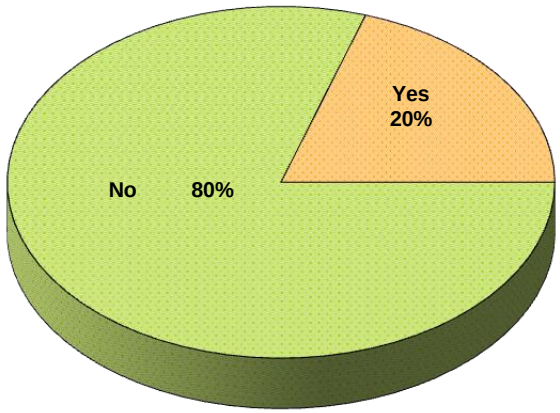


Figure 27: Intubated

All the patients were intubated orally. A total of 20% of the patients required intubation and subsequent ventilator support. 80% of the patients did not require ventilation.

Of the patients who were ventilated,

- 8 of the 11 patients were intubated on day 1 of poisoning.
- 2 patients were intubated on day 3
- one patient on the day 2 of admission.

TABLE 31: TOTAL ICU LENGTH OF STAY

ICU length of stay	Number of patients	%
1-2 days	1	1.8
3-7 days	33	60
>7 days	21	38.2
Total	55	100

Mean ± SD: 6.15±2.85

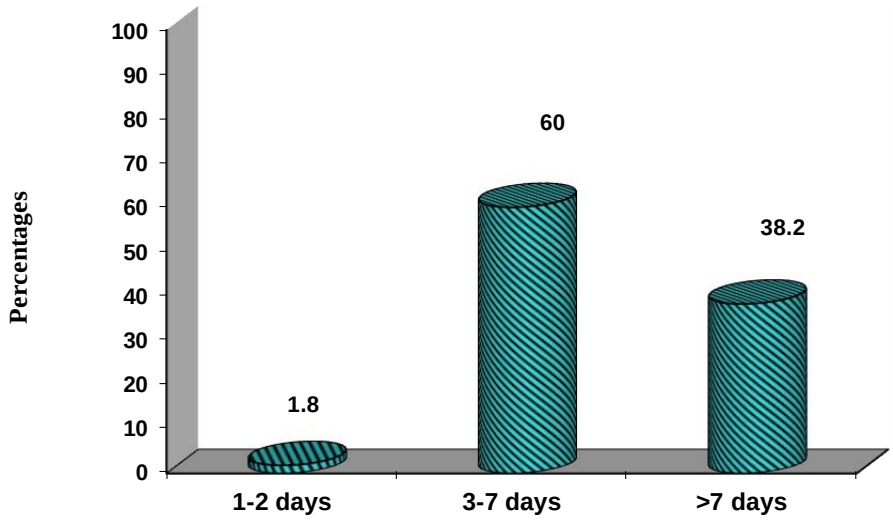


Figure 28: ICU length of stay

All acute organophosphorous poisoning patients were admitted to the medical ICU as a hospital protocol. The mean ICU length of stay was 6.15 days. The least duration of ICU stay was 1 day and the maximum was 16 days. 60% of the patients were in the ICU between 3-7 days.

TABLE 32: TOTAL HOSPITAL DURATION OF STAY

Hospital stay	Number of patients	%
<7 days	3	5.45
7-14 days	47	85.45
>14 days	5	9.1
Total	55	100

Mean ± SD: 9.73±5.56

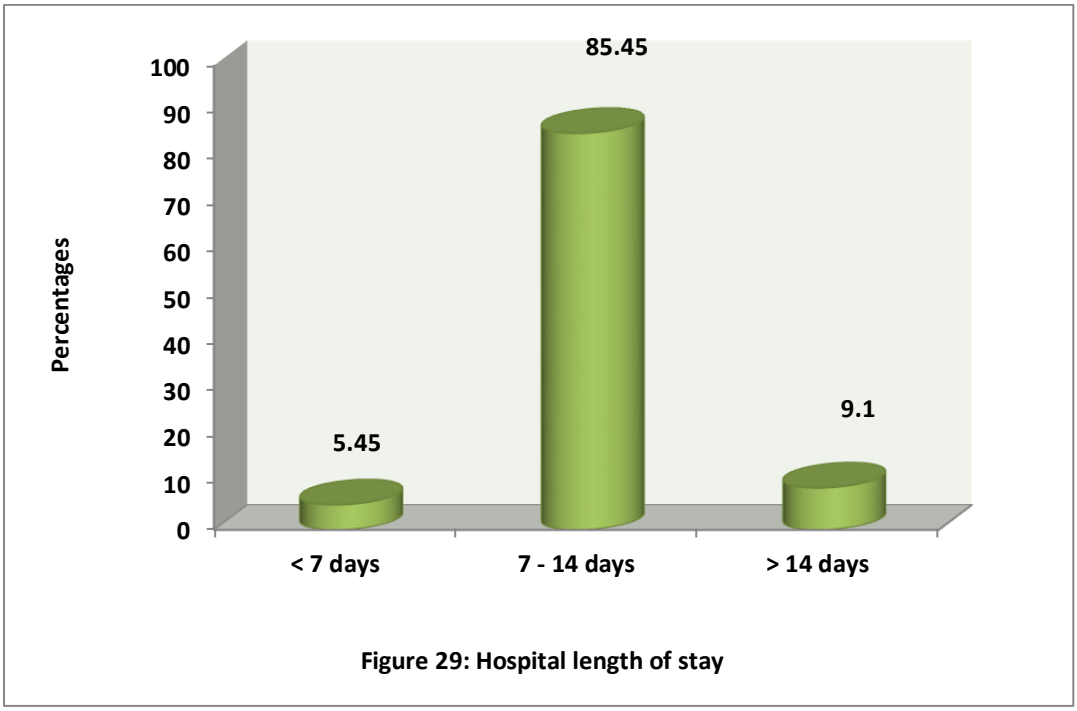
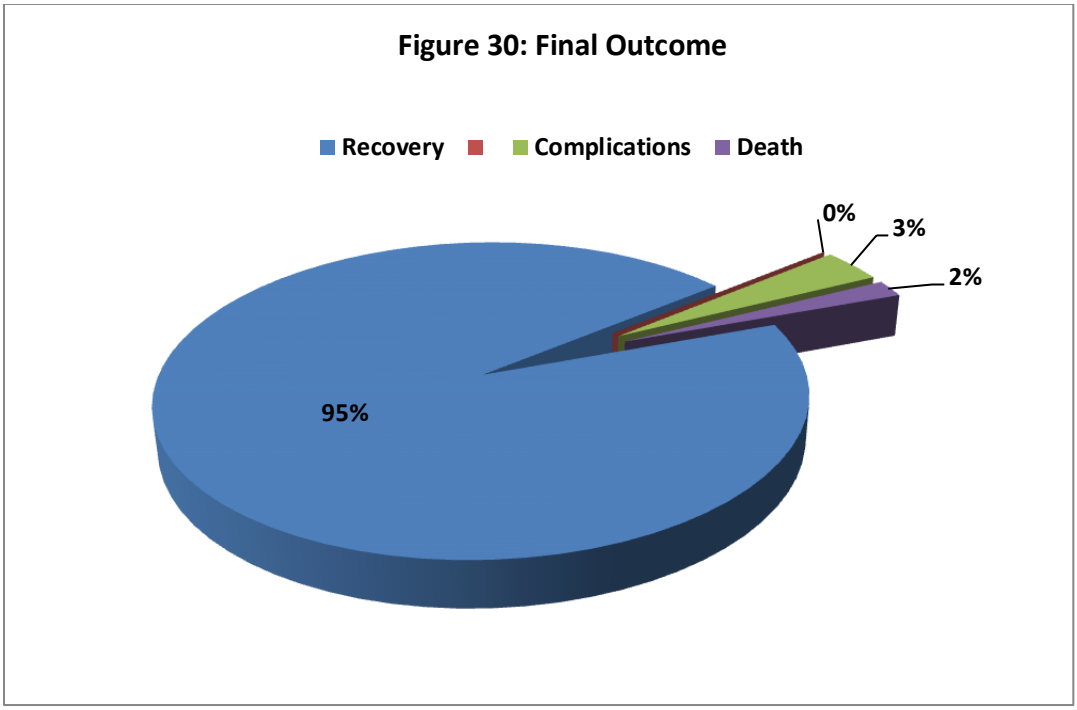


Figure 29: Hospital length of stay

The mean duration of hospital stay was 9.73 days. The minimum period of stay was 5 days and the maximum was 44 days. 86% of the patients were in the hospital between 7 – 14 days.

TABLE 33: FINAL OUTCOME OF THE PATIENT

Outcome	Number of patients	%
Recovery	52	94.6
Complications	2	3.6
Death	1	1.8
Total	55	100



In our study, 94.6% of the patients recovered completely and only one patient succumbed. 3.6% (n=2) developed complications (ventilator associated pneumonia and renal failure), but eventually recovered from the same.

DISCUSSION

Acute Organophosphorous compound poisoning is one of the most frequent poisonings encountered in our centre with the total number of adult cases admitted being 292 over a period of one year. 80% are mixed poisonings and isolated Organophosphorous Poisoning comprised of 20% of the cases (n=60).

All the patients presented with a suicidal mode of poisoning

COMPARATIVE DISCUSSION

Age of the patients

Of the 55 cases studied over a period of one year, majority of the patients were in the age group of 21-30 years (55%). This correlates with other studies as shown below. In the age group of 21 – 30 years, such an impulsive and irresponsible action probably shows an immaturity of mind and an attempt to draw attention.

Authors	Sample size	Age group (years)	Percentage	Mean age (years)
Present study	55	21 – 30	55	28.33
Kar et al[103]	100	21 – 30	42	29.02
Sam et al[104]	71	21 – 30	40	31.23

Gender Distribution

In the present study, 67% of the patients were males and the male to female ratio was 2.1:1. This correlates with the findings of the other studies as shown below. impulsive, intentional poisoning due to occupational stress and as more men are employed in the agriculture industry, this could explain the increased prevalence of

poisoning amongst men. However, in a study done by M. Vishwanathan et al[60], 66% of the patients who consumed organophosphorous compound were females.

Authors	Male (%)	Female (%)	M:F
Present study	67.3	32.7	2.1:1
Shankar P S et al[105]	59.87	40.2	1.48:1
Goel et al[78]	71.85	28.15	2.5:1
Kar et al[103]	68	32	2.2:1
Sam et al	76	23.9	3.2: 1
Bannerjee I et al[106]	41.43	58.57	1:1.38

Occupation of the patients

39.9 % of the patients were agriculturists which explain their easy access to insecticides. The next group was students who indulged in self poisoning impulsively. 45.5% of the entire group was literates and 54.5% were illiterates.

In contrast to our study, Bannerjee I et al[106] showed that majority of the patients were housewives (42%) followed by farmers (33.99%), shopkeepers (9.93%), laborers (8.14%), students (6.2%).

Intention of Poisoning

All were suicidal poisonings and this form of poisoning is more common in developing countries.[19,76] As OP compounds are generally available ready hand as pesticides and open access to these compounds at pesticide shops may be the reason for OP compounds to be used as a common mode of suicidal attempt. Also, the general

knowledge about this compound being a poison, lethal to humans, is common even amongst illiterates. This is in comparison to values reported by Reihman et al[107], Noiura et al[87] (90%), Goel et al[78] (96.1%) and Gupta et al[108] (91%). In contrast, figures from developed countries like Japan, show accidental exposure forms a major bulk of organophosphorous compound poisoning cases.[11,29]

Type of Poison Consumed

Chlorpyriphos was the most common poison consumed in our study with an incidence of 49% of the total cases. This compound is commonly marketed as a pesticide spray in our area.

The most commonly implicated compound in other studies with their incidence is given below:

Authors	**Compound**	**Incidence**
Present study	Chlorpyriphos	49%
Bannerjee I et al[106]	Methyl Parathion	35.74%
Sam et al	Methyl Parathion	40.8%

In a study conducted in Nepal,[107] Methyl parathion (64.62%) was the most common one followed by Baygon spray, Malathion, Dichlorvos. Methyl parathion was also the most common poison in studies conducted in Chennai.[47] However, in a study conducted in Turkey,[46] Dichlorvos was the most common one. This variation in the type of poison consumed can be attributed to the regional availability of pesticides in different countries.

Pre-hospitalization Period

The interval period between consumption of the compound and receiving treatment has been found to influence outcome in many studies.[48]

Majority of the patients in our study presented between 4 -5 hours post-exposure. The average interval period in our study was found to be 3 hours 37 minutes. The shortest interval period was 15 minutes and the longest was 16 hours. Our hospital is a rural tertiary care centre situated approximately 5 kilometres away from the nearest town. This could be one of the reasons for delayed presentation to our centre.

In the study done by Bannerjee et al[106], the mean interval between poison consumption and admission to the hospital was 4.4 hours. In studies conducted at Chennai,[47] maximum patients (89.69%) presented within 6 hours.

ANALYSIS OF THE STUDY

Quantity of poison consumed

In our study, the majority of the patients (56.4%) had consumed less than 50 ml of the compound. Only 38.2% consumed about 100 ml. This was enquired into either at admission or after recovery, in case the patient was obtunded on admission. As all the cases in our study were intentional and impulsive, consuming more than 50 ml (half a glass) neat / straight from the bottle might be difficult due to the offensive smell and taste. Also, suicidal poisoning is mostly used by youngsters as a mode to threaten others and hence a small dose would suffice for the purpose.

Pattern of Consumption of Poison

78.2% of our patients consumed the compound directly from the bottle and 12.7% of the patients consumed it along with alcohol. A total of 10 patients in our study were prior alcoholics. Amongst the 10, only 7 consumed the poison with alcohol. Direct consumption from the bottle reflects impulsiveness and those who consumed with alcohol show that it is a pre-meditated action.

There is no comparative study available on the impact of alcohol on OPC poisoning.

Presence of Cholinergic Symptoms

Only 72.7% of the patients manifested with cholinergic symptoms at the time of presentation. The most common symptom was vomiting. All patients in our study had the characteristic smell of OPC poisoning. The signs commonly seen amongst our patients were fasciculations, miosis and sweating. None of the patients had seizures. These findings are similar to other studies.[107,108]

DISCUSSION ON SEVERITY

Severity assessment using scoring systems

Glasgow coma scale

74.5% of the patients had a GCS of more than 13. Only 9.1% of the patients had a GCS score of less than 8. Of these, only 2 patients had consumed poison with alcohol.

Table 34: Correlation of clinical parameters with GCS scores

Parameter	GCS < 8	GCS : 9-12	GCS 13 -15
N	5	41	9
%	9.1	16.4	74.5
Mean age	36.8	28.26	28.33
M:F	5:0	1.56:1	3.5:1
Most common compound consumed n (%)	METHYL PARATHION 2 (40%)	CHLORPYRIPHOS 25 (61%)	PHORATE 3 (66.7%)
Mean pre-hospitalization period	5 hours 29 minutes	2 hours 34minutes	3 hours 37 minutes
Co-ingestion with alcohol	40% (n=2)	7.4% (n=3)	22.3% (n=2)
Presence of cholinergic symptoms	80% (n=4)	68.3% (n=28)	88.9% (n=8)
Mean RBS levels	140.2	109.6	147.5
Mean pseudocholinesterase level at admission	722.4	2208.29	808
Mean duration of atropine administered (days)	7.2	5.24	7.2
Required intubation on admission (n)	4 (80%)	3 (7.4%)	2 (22.3%)
Mean ICU length of stay (days)	8.4	5.41	7.3
Outcome: recovered (n)	4 (80%)	41 (100%)	7 (80%)
Outcome: complications (n)	1	0	1
Outcome: death (n)	0	0	1

In our study, patients with a low GCS (<8) were found to be of an average 36 years of age with male preponderance, pre-hospitalization period averaging to about 5 hours. 40% had co-ingested alcohol, 80% had cholinergic symptoms.

The average pseudocholinesterase was lower in the low GCS group and this was statistically significant ($p \leq 0.001$). The duration of atropine administered and the mean RBS levels did not vary between the 3 groups. 80% of the patients with low Glasgow scores required intubation on admission and this was statistically significant ($p \leq 0.001$). Their mean ICU length of stay was also found to be higher. The outcomes of the patients were on an average > 80% in all the three groups. However, the patient who succumbed had a GCS of more than 13.

In a study done by Sam et al, the GCS score of less than eight was observed in 23 (32.4%) patients. A total of 40 (56.3%) patients required intubation and ventilator assistance, of whom 15 patients had a GCS score of <8, while 11 had a GCS score of 66.

POISONING SEVERITY SCORE

Majority of the patients had minor scores (47.3%) at admission. Only 4 patients (7.3%) had severe scores on admission.

Table 35: Correlation of clinical parameters with PSS scores

Parameter	NONE	MINOR	MODERATE	SEVERE
N	2	26	23	4
%	3.6	47.3	41.8	7.3
Mean age (years)	21	26.7	30.9	37.5
M:F	2:0	1:1	3.6:1	4:0
Most common compound consumed n (%)	Chlorpyriphos and phorate	Chlorpyriphos 16(61.6%)	Chlorpyriphos 10 (43.5%)	Quinalaphos 2 (50%)
Mean pre hospitalization period	2 hours 30 minutes	3 hours 27 minutes	3 hours 41 minutes	4 hours 51 minutes
Co-ingestion with alcohol n (%)	0	2 (7.7%)	3 (13.1%)	2 (50%)
Presence of cholinergic symptoms n;%	0	16; 61.6%	20; 87%	4; 100%
Mean pseudocholinesterase level at admission	200	1772.3	2338.4	290
Mean duration of atropine administered (days)	4	5.3	6.17	7
Required intubation on admission (n; %)	0	0	4 (17.4%)	4 (100%)
Mean ICU length of stay (days)	10	5.57	6.13	14.25
Outcome: recovered (n)	2	26	20	4
Outcome: complications (n)			2	
Outcome: death (n)			1	

Majority of the patients presented with minor scores. Males had more severe scores than females. The mean age at presentation was highest in the severe group. Chlorpyriphos was the commonest poison consumed. Amongst the 4 patients who presented with severe scores, 50% of them had consumed Quinalaphos. The mean pre-hospitalization period was also higher in the severe group. Also, patients in the severe group required longer duration of atropine. This group was also associated with a 100% requirement of ventilator support and this was found to be statistically significant ($p = <0.001^{**}$). The patients in the severe group also had prolonged periods of ICU stay, but recovered completely.

A study by Pach et al (1999)[109] has reported that the PSS is useful in assessing severity on the basis of observed clinical signs and symptoms (at their maximum), but does not take into account potential risks or plasma/ serum concentrations of the poison.

APACHE III SCORE

Table 36: Correlation of clinical parameters with APACHE III scores

Parameter	Less than 60	More than 60
N	45	10
%	81.8	18.2
Mean age (years)	26.9	38.6
M:F	2:1	2.3:1
Most common compound consumed n (%)	Chlorpyriphos 26 (57.8%)	Phorate 4 (40%)
Mean pre hospitalization period	3 hours 19 minutes	4 hours 58 minutes
Co-ingestion with alcohol (n; %)	4	3
Presence of cholinergic symptoms	32	8
Mean pseudocholinesterase level at admission	1842.3	1852
Mean duration of atropine administered (days)	5.5	6.8
Required intubation on admission n (%)	4 (2.3%)	7 (70%)
Mean ICU length of stay (days)	5.7	7.4
Outcome: recovered (n)	43	9
Outcome: complications (n)	1	1
Outcome: death (n)	1	0
Mean predicted mortality rate	0.85	5.35

Majority of the patients in our study had normal APACHE scores. Those with high scores were only 18%, mostly men with an average age group of 38 years. In contrast to all other results, Phorate was the most common compound implicated in higher APACHE scores. The mean pseudocholinesterase levels were also normal

amongst the two groups. 70% of the patients in the high score group required intubation on admission and this was found to be statistically significant (p = <0.001). The mean predicted mortality rate was 5.35 in the high score group, but the actual mortality rate was nil as none of the patients in this group succumbed. This can be attributed to better care and management.

PREDICTORS OF PROGNOSIS

Plasma Pseudocholinesterase Levels and Prognosis

The plasma pseudocholinesterase levels were estimated at admission and on days 3.5 and 7. The mean levels were the least on the day of admission and gradually increased by day 7. A low value on day 7 is a marker of severity and is found to be statistically significant (p = <0.001).

Table 37: Serum Pseudocholinesterase Evaluation

Variables	Day 1	Day 3	Day 5	Day 7
Minimum-Maximum	128-13000	200-11000	200-10923	200-8776
Mean ± SD	1844.07±2431.34	1880.49±2233.87	2328.07±2244.83	3216.13±2474.51
P value from day1	-	0.677	0.003**	<0.001**

As a marker of assessing requirement of ventilator assistance, pseudocholinesterase levels on days 1, 3, 5 are suggestive to be significant. Amongst those patients who were intubated on admission, the mean pseudocholinesterase levels were found to be the least.

Table 38: Assessment of incidence for intubation with serial pseudocholinesterase monitoring

Variables	Incidence of intubation		p value
	No	Yes	
PCHE (day 1)	2117.19±377.31	679.42±242.55	0.066+
PCHE (day 3)	2137.77±349.06	936.67±304.14	0.097+
PCHE (day 5)	2593.56±354.28	1296.75±366.72	0.075+
PCHE (day 7)	3446.25±380.39	2113.3±634.94	0.125

Approximately 44% of the patients who presented with low serum levels were in their second decade, with male preponderance. 41% of the patients who consumed chlorpyriphos had low pseudocholinesterase levels on admission.

Contrary to the expected range, patients with normal GCS values had an average lower pseudocholinesterase levels than those with low GCS. However, none of these values were statistically significant.

Table 39: Correlation of Clinical Variables with Severity of Poisoning Determined by Admission Pseudocholinesterase levels

Variables	Severity of poisoning			p value
	<1000 (n=32)	1000-3000 (n=12)	>3000 (n=11)	
Age in years				
• <=20 years	10(29.4%)	3(21.4%)	1(8.3%)	0.386
• 21-30	13(44.1%)	5(50%)	7(66.7%)	
• 31-40	5(14.7%)	3(21.4%)	0(0%)	
• >40 years	4(11.8%)	1(7.1%)	3(25%)	
Gender				
• Male	20(64.7%)	10(85.7%)	7(58.3%)	0.250
• Female	12(35.3%)	2(14.3%)	4(41.7%)	
OP compound				
• Chlorpyriphos	14(41.2%)	7(57.1%)	5(50%)	0.838
• Phorate 10%	6(17.6%)	2(21.4%)	2(25%)	
• Monocrotophos	4(14.7%)	0(0%)	1(8.3%)	
• Dimethoate	2(5.9%)	2(14.3%)	1(8.3%)	
• Quinalaphos	3(11.8%)	1(7.1%)	0(0%)	
• Methylparathion	3(8.8%)	0(0%)	1(8.3%)	
Interval hours				
• <1	1(2.9%)	1(7.1%)	1(8.3%)	0.953
• 1-2	5(14.7%)	2(21.4%)	2(16.7%)	
• 2-3	8(29.4%)	2(14.3%)	2(16.7%)	
• 3-4	5(14.7%)	2(21.4%)	1(8.3%)	
• 4-5	7(20.6%)	3(21.4%)	3(33.3%)	
• >5	6(17.6%)	2(14.3%)	2(16.7%)	
Quantity				
• <50 ml	18(55.9%)	6(50%)	7(66.7%)	0.958
• 50-100 ml	2(5.9%)	1(7.1%)	0(0%)	
• 100 ml	12(38.2%)	5(42.9%)	4(33.3%)	
• Ingested with Alcohol	4(11.8%)	1(7.1%)	0(0%)	0.356

Variables	Severity of poisoning			p value
	<1000 (n=32)	**1000-3000 (n=12)**	**>3000 (n=11)**	
GCS				
• <8	4(11.8%)	1(7.1%)	0(0%)	0.412
• 9-12	8(23.5%)	1(7.1%)	1(8.3%)	
• 13-15	20(64.7%)	10(85.7%)	10(91.7%)	
PSS				
• None	2(5.9%)	0(0%)	1(8.3%)	0.470
• Minor	14(47.1%)	4(35.7%)	6(50%)	
• Moderate	12(35.3%)	8(64.3%)	4(41.7%)	
• Severe	4(11.8%)	0(0%)	0(0%)	
APACHE score				
• >60	7(20.6%)	1(7.1%)	1(8.3%)	0.377
TROP T				
• Positive	7(20.6%)	3(21.4%)	1(8.3%)	0.733

INFLUENCE OF METABOLIC PARAMETERS ON PROGNOSIS

Random Blood Sugar Levels

Table 40: Studies Comparing Hyperglycemia

Authors	Mean sugar levels (mg/dl)	% of patients with hyperglycemia
Present study	118.6	25.4
Sungur et al[110]	131	32
Shobha et al[49]		69

Hyperglycemia in acute OPC poisoning has been reported many times in literature.[49,110] In our study, the mean sugar levels were found to be 118.6 and 25.4% had hyperglycemia (RBS > 140 mg/dl) and 18.2% had hypoglycemia (RBS <75 mg/dl).

The mean RBS level was in the hyperglycemia range amongst those who were mechanically ventilated on admission & in the patient who succumbed. But this was not found to be statistically significant

Table 41: Comparison between mean sugar levels amongst those requiring ventilation on admission

Variable	Not intubated	Intubated at admission	p value
n	44	11	0.131
%	80	20	
MEAN RBS (mg/dl)	111.94	141.58	

Table 42: Comparison of mean sugar levels vs. outcome of the patients

Variable	Recovery	Complication	Death	p value
n	52	2	1	0.579
%	94.6	3.6	1.8	
Mean RBS (mg/dl)	117.05	124.5	187	

Serum Amylase Levels

The normal range of serum Amylase is < 130 U/L. we had 9 patients with hyper-amylasemia at admission. The average amylase levels amongst all the patients were found to be 88.05 U/L.

Table 43: Comparison between Mean Amylase Levels amongst Those Requiring Ventilation on Admission

Variable	Not intubated	Intubated at admission	p value
n	44	11	0.708
%	80	20	
Mean Amylase (U/L)	82.65	88.67	

Table 44: Comparison of Mean Amylase Levels Vs Outcome of the Patients

Variable	Recovery	Complication	Death	p value
n	52	2	1	0.497
%	94.6	3.6	1.8	
Mean Amylase (U/L)	87.38	126.5	46	

Serum amylase levels did not seem to show any correlation with either the need for ventilator support or with respect to outcome of the patient. The mean RBS levels amongst those with hyperamylasemia was found to be 90.11. This is contradictory to the study done by Matsumiya et al which has showed that an increase in plasma amylase above the normal range on the day of admission was related to the development of respiratory failure.

Arterial Blood Gas Analysis

40% of the patients had metabolic acidosis and 32.7% had mixed acidosis. There have been earlier case reports of metabolic acidosis with hypotension on acute OPC poisonings.[111-114] None of our patients had hypotension at presentation. All the patients with metabolic acidosis recovered completely even though 5 (22.8%) patients required ventilator support at admission.

Acute respiratory acidosis can occur in the event of respiratory failure. 60% of the patients who presented with acute respiratory acidosis required ventilator support on admission. However, this was not found to be statistically significant.

Creatinine Phosphokinase (CPK)

50.9% (n = 28) of the patients had elevated CPK levels and 49.1% (n = 27) had normal levels.

Table 45: Comparison of Elevated CPK Levels with Severity and Outcome

Parameters	n	%	p value
Intubated at Admission	7	30	0.536
Recovery	26	92.9	
Complications	2	7.1	
Death	0		

We found no difference between elevated CPK levels and either severity or outcome. Several animal model studies on rat liver and fresh-water snails indicate the association between severe OP poisoning and CPK levels.[115] In a study by Agarwal et al, it was proposed that serum level of CPK is often found to be elevated in OP poisoning and may be used as a biomarker.[116]

ICU Length of Stay

The mean ICU length of stay was found to be 6 days. The duration of stay was found to be more for patients who were intubated at admission and this was found to have moderate significance ($p = 0.022$*).

DISCUSSION ON COMPLICATIONS

Cardiotoxicity in Acute OPC Poisoning

We evaluated for cardiotoxicity by estimating baseline CKMB levels, Troponin T assay within 12 hours of admission and by monitoring ECG changes. Positive troponin T was noted in 9 patients (16.4%). Elevated CKMB levels were seen in 39 patients (70.9%).

The main cardiac rhythm abnormality seen in our study was sinus tachycardia (n=18; 32.8%). Sinus tachycardia, seen in organophosphate poisoning can be attributed to nicotinic effect, while sinus bradycardia is due to cholinergic manifestations.[117] We also had one patient presenting with an RBBB pattern and one patient having extrasystoles.

Table 46: Correlation between Elevated CKMB, Positive Troponin, ECG Changes with Requirement of Ventilatory Support on Admission

PARAMETERS	n	%	p VALUE
Positive Troponin T (n=9)	6	66.7	0.005**
CKMB > 24 (n=38)	11	29	0.004**
ECG : Tachycardia (n=19)	7	36.9	0.007**
Mean CKMB Levels	98.7		<0.001**

In our study, positive troponin T, elevated CKMB levels and ECG suggestive of tachycardia can be taken as markers of severity as they indicate cardiotoxicity and are found to have statistical significance towards need for intubation.

Table 47: Correlation between Elevated CKMB, Positive Troponin, ECG Changes with Outcome of the Patient

Parameters	Recovery	Complications	Death	p value
Positive Troponin T (n=9)	7 (77.8%)	1	1	0.021*
CKMB > 24 (n=38)	36 (94.8%)	1	1	0.100
ECG : Tachycardia (n=19)	17 (89.5%)	1	1	0.576
Mean CKMB Levels	56.51	126	147	0.378

In our study, positive troponin T was significantly associated with outcome of the patient. The mean CKMB level was also found to be highest in the patient who died, but this was not statistically significant.

Hence, we can conclude that amongst the markers we took to predict cardiotoxicity, troponin T is significantly associated with need for ventilator support and also significantly affects outcome of the patient.

Factors Predicting the Need for Mechanical Ventilation at Admission

In our study, 11 patients (20%) required mechanical ventilation. Amongst these, 8 were intubated at presentation and 2 patients on day 2 and 1 on day 3 respectively. The average duration of mechanical ventilation was 3.81 days. The mean ICU length of stay in this group was 7.54 days. Of the 11 patients, 1 patient died and 2 developed complications.

Table 48: Correlation of Clinical Variables with Incidence of Intubation

Variables	Incidence intubation		p value
	No (n=44)	Yes (n=11)	
Age in years			
• 31-40	2(4.2%)	6(50%)	<0.001**
Gender			
• Male	31(64.6%)	10(83.3%)	0.306
• Female	17(35.4%)	2(16.7%)	
OP compound			
• Chlorpyriphos	25(52.1%)	3(25%)	0.030*
• Dimethoate	5(10.4%)	0(0%)	
• Methylparathion	1(2.1%)	3(25%)	
Interval hours			
• <1	2(4.2%)	1(8.3%)	0.137
• >5	7(14.6%)	3(25%)	
Quantity			
• <50 ml	27(56.3%)	7(58.3%)	0.756
• 100 ml	19(39.6%)	4(33.3%)	
Ingested with			
• Alcohol	5(10.4%)	2(16.7%)	0.598
Cholinergic symptoms			
• Yes	32(66.7%)	10(83.3%)	0.317
GCS			
• <8	1(2.1%)	4(33.3%)	<0.001**
PSS			
• Moderate	18(37.5%)	8(66.7%)	<0.001**
• Severe	0(0%)	4(33.3%)	
APACHE score			
• >60	2(4.2%)	7(58.3%)	<0.001**

Variables	Incidence intubation		P value
	No (n=44)	Yes (n=11)	
PCHE score			
• <1000	24(50.0%)	10(83.3%)	0.007**
• 1000-3000	12(25.0%)	2(16.7%)	
• >3000	12(25.0%)	0	
TROP T			
• Positive	5(10.4%)	6(50%)	0.005**
CKMB			
>25	27 (71%)	11 (29%)	0.004**

Table 49: Comparison of Mean Study Parameters according to Incidence of Intubation

Variables	Incidence of intubation		p value
	No	Yes	
Age in years	26.85±1.54	37±3.07	0.005**
Interval hours of admission	3.83±0.21	3.92±0.51	0.865
APACHE score	39.35±1.54	62.08±5.05	<0.001**
APS score	38.88±1.45	59.5±5.94	<0.001**
RBS	111.94±8.79	141.58±16.18	0.131
S amylase	82.65±7.51	88.67±10.64	0.708
CPK	381.25±61.63	302.67±49.25	0.536
CKMB	35.96±3.83	89.67±16.75	<0.001**
PCHE –day1	2117.19±377.31	679.42±242.55	0.066+
PCHE –day3	2137.77±349.06	936.67±304.14	0.097+
PCHE –day5	2593.56±354.28	1296.75±366.72	0.075+
PCHE –day7	3446.25±380.39	2113.3±634.94	0.125
Atropine duration	5.46±0.31	7.08±0.57	0.022*
ICU stay in days	5.63±0.32	8.25±1.17	0.003**
Total hospital stay in days	9.38±0.83	11.17±1.30	0.322

The factors which significantly influenced need for ventilator support on admission were:

- Age between 31-40 years
- A GCS of < 8 on admission
- PSS of moderate
- APACHE score of > 60
- Pseudocholinesterase level of < 1000 at presentation
- Positive troponin T
- Elevated CKMB levels

Other factors which can be used to predict need for ventilator support on admission, but were not found to be statistically significant were –

- Male gender (83.3%).
- 25% possibility each with ingestion of either chlorpyriphos or cypermethrin.
- 25% of patients with a delayed presentation of > 5 hours.

TREATMENT ANALYSIS

Duration of Atropine

The average atropine duration was 5.74 days. Amongst the patients who were intubated at admission, the mean duration was 7.08±0.57 and this was found to be moderately significant. The mean duration of atropine administered was more amongst those patients who had a low pseudocholinesterase level on admission. But this was not found to be statistically significant.

Table 50: Correlation between Mean Atropine Duration with Intubation on Admission and Pseudocholinesterase Level on Admission

Parameters	Mean atropine duration (days)	p value
Incidence of intubation		
Yes	7.08±0.57	0.022*
No	5.46±0.31	
Pseudocholinesterase level on admission		
< 1000	6.18	
1000 – 3000	5.41	
>3000	4.81	0.104

OUTCOME PREDICTION

94.6% of the patients in our study recovered completely and were discharged. 2 patients (3.6%) developed complications (pneumonia), but subsequently recovered and were discharged. One patient died on day 7 of hospital stay.

Table 51: Correlation of Clinical Variables with Outcome

Clinical variables	Outcome			p value
	Recovery (n=52)	Complications (n =2)	Death (n =1)	
Interval hours				
• <1	2(3.8%)	0(0%)		0.002**
• 1-2	9(17.3%)	1 (50%)		
• 2-3	12(23.1%)	0(0%)		
• 3-4	7(13.5%)	0(0%)		
• 4-5	13(25%)	1 (50%)		
• >5	9(17.3%)	0	1 (100%)	
GCS				
• <8	4(7.7%)	1(50 %)		0.039*
• 9-12	7(13.5%)	1(50 %)	1 (100%)	
• 13-15	41(78.8%)	0(0%)		
PSS				
• None	2(3.8%)	0(0%)		0.016*
• Minor	26(50%)	0(0%)		
• Moderate	20(38.5%)	2(100%)	1 (100%)	
• Severe	4(7.7%)	0(0%)		
APACHE score				
• <40	24(46.2%)	0(0%)		0.102
• 40-50	16(30.8%)	1(33.3%)		
• 50-60	5(9.6%)	1(33.3%)		
• >60	7(13.5%)	1(33.3%)		
Intubation				
• No	43(82.7%)	1(33.3%)		0.146
• Yes	9(17.3%)	2(66.7%)		

A pre-hospitalization period of more than 5 hours is significantly associated with mortality. A GCS score of 9-12 and a PSS of moderate has moderate significance to outcome.

CONCLUSION

Acute OPC poisoning is one of the most common medical emergencies encountered in our hospital.

The mean age at presentation was around 28 years.

The incidence is found to be twice more common among men and the reason being suicidal.

The most common compound consumed was Chlorpyriphos (about 50 ml), with or without alcohol.

A pre-hospitalisation period of more than 5 hours is significantly associated with low Glasgow Coma Scale, severe Poisoning Severity Scores; plasma Pseudocholinesterase level of less than 1000 U/l at presentation, positive Troponin T assay on admission and mortality.

Almost all patients had significant recovery without any residual deficit. Only a single death occurred due to concomitant alcohol intoxication.

SUMMARY

A total of 55 patients were studied over a period of one year. Majority of the patients were in the age group of 21-30 years (55%) . 67% of the patients were males and the male to female ratio was 2.1:1. All were suicidal poisonings.

Chlorpyriphos was the most common poison consumed in our study.Majority of the patients in our study presented between 4 -5 hours post-exposure. The average interval period in our study was found to be 3 hours 37 minutes. The majority of the patients (56.4%) had consumed less than 50 ml of the compound. Most of our patients consumed the compound directly from the bottle. Only 72.7% of the patients manifested with cholinergic symptoms at the time of presentation. The most common symptom was vomiting. All patients in our study had the characteristic smell of OPC poisoning.

The average pseudocholinesterase was lower in the low GCS group and this was statistically significant. Males had more severe PSS scores than females. Patients in the severe group required longer duration of atropine. This group was also significantly associated with requirement of ventilator support. The patients in the severe group also had prolonged periods of ICU stay, but recovered completely. Most of the patients in the high score group required intubation on admission and this was found to be statistically significant. The mean levels of pseudocholinesterase were the least on the day of admission and gradually increased by day 7. A low value on day 7 is a marker of severity and is found to be statistically significant.

In our study, positive troponin T, elevated CKMB levels and ECG suggestive of tachycardia can be taken as markers of severity as they are found to have statistical significance towards need for intubation.

The factors which significantly influenced need for ventilator support on admission were:

- Age between 31-40 years
- A GCS of < 8 on admission
- PSS of moderate
- APACHE score of > 60
- Pseudocholinesterase level of < 1000 at presentation
- Positive troponin T
- Elevated CKMB levels

A pre-hospitalization period of more than 5 hours is significantly associated with mortality. A GCS score of 9-12 and a PSS of moderate has moderate significance to outcome.

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ANNEXURE I

GLASGOW COMA SCALE

Standard Glasgow Coma Scale

Eye opening	Best verbal response	Best motor response
4 : spontaneous 3 : to speech 2 : to pain 1 : none	5 : oriented 4 : confused 3 : inappropriate words 2 : incomprehensible sounds 1 : none	6 : obeys commands 5 : localizes 4 : withdraws 3 : abnormal flexion 2 : extension 1 : none
TOTAL GCS SCORE : 3-15		

ANNEXURE II

POISONING SEVERITY SCORE

ANNEXURE III

APACHE III SCORING SYSTEM

ANNEXURE IV

PROFORMA

(A) IDENTIFICATION DETAILS

SERIAL NO:

NAME:

AGE/SEX: HOSP NO. :

ADDRESS: OCCUPATION:

DATE & TIME OF ADMISSION:

(B) PRESENTING COMPLAINTS:

- NAME OF OP COMPOUND [INCLUDING COMPOSITION]:
- MODE OF EXPOSURE:
- DATE & TIME OF EXPOSURE:
- INTERVAL BETWEEN EXPOSURE AND INITIATION OF THERAPY (hrs):
- QUANTITY INGESTED:
- IF INGESTED, RAW INGESTION OR WITH: ALCOHOL / WATER / KEROSENE / AERATED DRINK / Others:
- H/O : VOMITTING / SEIZURES / TREMORS / ALTERED SENSORIUM / DYSPNOEA Others (specify) -

(C) PAST H/O

- DM / HTN / IHD / PTB / COPD / BA / CLD / Others.....
- H/O previous suicidal attempts – YES / NO; If YES, details -

(D) PERSONAL H/O

- SMOKING / ALCOHOL / Paan chewing / IVDA /_____
- BOWEL / BLADDER HABITS-
- Other habits:

Eye opening	
Spontaneous	4
To verbal command	3
To pain	2
None	1
Verbal response	
Oriented – converses	5
Disoriented – converses	4
Inappropriate words	3
Incomprehensible	2
No response	1
Motor response	
Obeys verbal commands	6
Localizes to painful stimuli	5
Flexion withdrawal	4
Abnormal flexion	3
Extension	2
No response	1

(E) PHYSICAL FINDINGS

- GCS Score :
- VITAL SIGNS:
  - Pulse rate & rhythm:
  - BP: _____mm Hg in Right upper limb, supine
  - Respiratory rate & type:
  - Temperature:
- Pupils:
- Secretions : YES / NO
- Bowel incontinence – YES / NO
- Bladder incontinence – YES / NO

(F) SYSTEMIC EXAMINATION:

ORGAN	NONE	MINOR	MODERATE	SEVERE
	0	1	2	3
	No symptoms or signs	Mild, transient, and spontaneously resolving symptoms or signs	Pronounced or prolonged symptoms or signs	Severe or life-threatening symptoms or signs
GI-tract		• Vomiting, diarrhea, pain • Irritation, 1st degree burns, minimal ulcerations in the mouth • Endoscopy: Erythema, edema	• Pronounced or prolonged vomiting, diarrhea, pain ileus • 1st degree burns of critical localization or 2nd and 3rd degree burns in restricted areas • Dysphagia • Endoscopy: Ulcerative transmucosal lesions	• Massive hemorrhage, perforation • More widespread 2nd and 3rd degree burns • Severe dysphagia • Endoscopy: Ulcerative transmural lesions, circumferential lesions, perforation
Respiratory system		• Irritation, coughing, breathlessness, mild dyspnea, mild bronchospasm • Chest X ray: Abnormal with minor or no symptoms	• Prolonged coughing, bronchospasm, dyspnea, stridor, hypoxemia requiring extra oxygen • Chest X ray: Abnormal with moderate symptoms	• Manifest respiratory insufficiency (e.g., severe bronchospasm, airway obstruction, glottal edema, pulmonary edema, ARDS, pneumonitis, pneumonia, pneumothorax) • Chest X ray: Abnormal with severe symptoms
Nervous system		• Drowsiness, vertigo, tinnitus, ataxia • Restlessness • Mild extrapyramidal symptoms • Mild cholinergic/anticholinergic symptoms • Paresthesia • Mild visual or auditory disturbances	• Unconsciousness with appropriate response to pain • Brief apnea, bradypnea • Confusion, agitation, hallucinations, delirium • Infrequent, generalized, or local seizures • Pronounced extrapyramidal symptoms • Pronounced cholinergic/anticholinergic symptoms • Localized paralysis not affecting vital functions • Visual and auditory disturbances	• Deep coma with inappropriate response to pain or unresponsive to pain • Respiratory depression with insufficiency • Extreme agitation • Frequent, generalized seizures, status epilepticus, opisthotonos • Generalized paralysis or paralysis affecting vital functions • Blindness, deafness
Cardio-vascular system		• Isolated extrasystoles • Mild and transient hypo/hypertension	• Sinus bradycardia (HR～40–50 in adults, 60–80 in infants and children, 80–90 in neonates) • Sinus tachycardia (HR～140–180 in adults, 160–190 in infants and children, 160–200 in neonates) • Frequent extrasystoles, atrial fibrillation/flutter, AV-block Ⅰ-Ⅱ, prolonged QRS and QTc-time, repolarization abnormalities • Myocardial ischemia • More pronounced hypo/hypertension	• Severe sinus bradycardia (HR～<40 in adults, <60 in infants, <80 in neonates) • Severe sinus tachycardia (HR～>180 in adults, > 190 in infants and children, >200 in neonates) • Life-threatening ventricular dysrythmias, AV-block Ⅲ, asystole • Myocardial infarction • Shock, hypertensive crisis
Metabolic balance		• Mild acid-base disturbances (HCO_3^-～15–20 or 30–40 mmol/L, pH～7.25–7.32 or 7.50–7.59) • Mild electrolyte and fluid disturbances (K^+ 3.0–3.4 or 5.2–5.9 mmol/L) • Mild hypoglycemia (～50–70 mg/dL or 2.8–3.9 mmol/L in adults) • Hyperthermia of short duration	• More pronounced acid-base disturbances (HCO_3^-～10–14 or >40 mmol/L, pH～7.15–7.24 or 7.60–7.69) • More pronounced electrolyte and fluid disturbances (K^+ 2.5–2.9 or 6.0–6.9 mmol/L) • More pronounced hypoglycemia (～30–50 mg/dL or 1.7–2.8 mmol/L in adults) • Hyperthermia of longer duration	• Severe acid-base disturbances (HCO_3^-～<10 mmol/L, pH ～<7.15 or >7.7) • Severe electrolyte and fluid disturbances (K^+ <2.5 or >7.0 mmol/L) • Severe hypoglycemia (～<30 mg/dL or 1.7 mmol/L in adults) • Dangerous hypo- or hyperthermia
Liver		• Minimal rise in serum enzymes (AST, ALT ～2–5 × normal)	• Rise in serum enzymes (AST, ALT ～5–50 × normal) but no diagnostic biochemical (e.g., ammonia, clotting factors) or clinical evidence of liver dysfunction	• Rise in serum enzymes (～>50 × normal) or biochemical (e.g., ammonia, clotting factors) or clinical evidence of liver failure
Kidney		• Minimal proteinuria/hematuria	• Massive proteinuria/hematuria • Renal dysfunction (e.g., oliguria, polyuria, serum creatinine of ～200–500 μmol/L)	• Renal failure (e.g., anuria, serum creatinine of >500 μmol/L)

Blood		• Mild hemolysis • Mild methemoglobinemia (metHb ～10–30%)	• Hemolysis • More pronounced methemoglobinemia (metHb ～30–50%) • Coagulation disturbances without bleeding • Anemia, leucopenia, thrombocytopenia	• Massive hemolysis • Severe methemoglobinemia (metHb > 50%) • Coagulation disturbances with bleeding • Severe anemia, leucopenia, thrombocytopenia
Muscular system		• Mild pain, tenderness • CPK ～250–1500 IU/L	• Pain, rigidity, cramping, and fasciculations • Rhabdomyolysis, CPK ～1500–10,000 IU/L	• Intense pain, extreme rigidity, extensive cramping, and fasciculations • Rhabdomyolysis with complications, CPK ～> 10,000 IU/L • Compartment syndrome
Local effects on skin		• Irritation, 1st degree burns (reddening) or 2nd degree burns in <10% body surface	• 2nd degree burns in 10–50% of body surface (children: 10–30%) or 3rd degree burns in <2% of body surface	• 2nd degree burns in >50% of body surface (children: >30%) or 3rd degree burns in >2% of body surface
Local effects on eye		• Irritation, redness, lacrimation, mild palpebral edema	• Intense irritation, corneal abrasion • Minor (punctate) corneal ulcers	• Corneal ulcers (other than punctate), perforation • Permanent damage

(G) INVESTIGATIONS

DATE			
HB (gm %)		T. PROTEIN	
TC		ALBUMIN	
DC(N,L,E)		BILIRUBIN	
ESR		SGOT	
PLATELET COUNT		SGPT	
HCT			
BT		**ABG**	
CT			
PT		PH	
INR		PCO2	
APTT		PO2	
		HCO3	
RBS		SO2	
SODIUM			
POTASIUM		CPK	
S. AMYLASE		CKMB	
		TROP T	
HBsAG			
HIV		Urine R/M	

CHEST X RAY	
ECG	

PSEUDOCHOLINESTERASE LEVELS

	DAY 1	DAY 3	DAY 5	DAY 7
DATE→				
RESULT →				

PM FINDING: (In case of death)

CARDIAC HP		
VAGUS N HP		

OTHER INVESTIGATIONS (if any):

(H) TREATMENT GIVEN:

- IN EMERGENCY WARD
  - Oxygen saturation:
  - Oxygen given: YES / NO , if YES - _____L/min
  - PAM dose:
  - Atropine dose:
  - Other drugs:
  - Intubation done: YES / NO

- IN INTENSIVE CARE UNIT
  - FOR VENTILATED PATIENTS:
    - INTUBATED AT: EMERGENCY WARD / _____ DAY OF ADMISSION
    - TOTAL NUMBER OF DAYS OF VENTILATION :
  - ATROPINE & PAM DOSAGES:

DAY →	**D1**	**D2**	**D3**	**D4**	**D5**	**D6**	**D7**	**D8**	**D9**	**D10**	**TOTAL**
Atropine											
PAM											
Ventilation Status											

- OTHER DRUGS:
- Was blood / FFPs transfused during the course of therapy:

(I) OUTCOME OF TREATMENT : RECOVERY / DEATH / COMPLICATIONS (specify)

- DURATION OF ICU STAY:
- DATE OF DEATH / DISCHARGE:

(J) TOTAL DURATION OF HOSPITAL STAY:

(K) PSYCHIATRY DIAGNOSIS:

Psychiatric treatment:

Intentionality: suicidal / homicidal / accidental

(L) FINAL DIAGNOSIS:

ANNEXURE V

INFORMED CONSENT

I, _____ unreservedly in my full sense give my consent to take part in the study, the risks and benefits of which have been explained to me in my vernacular language.

Further I do not have any objections for the presentation of this study as a part of any publication.

Signature of witness

Signature of patient/guardian

KEY TO MASTER CHART

M	→	Male
F	→	Female
hrs.	→	Hours
ml	→	Millilitre
CHR	→	Chronic
H/o	→	History Of
GCS	→	Glasgow Coma Scale
PSS	→	Poisoning Severity Score
APACHE	→	Acute Physiology and Chronic Health Evaluation
PMR	→	Predicted Mortality Rate
ICU	→	Intensive Care Unit
LOS	→	Length of Stay
RBS	→	Random Blood Sugar
ABG	→	Arterial Blood Gas
CPK	→	Creatinine Phosphokinase
CKMB	→	Creatinine Kinase
PCHE	→	Pseudocholinesterase
CHR DEPRSN	→	Chronic Depression

MASTER CHART

SL NO	NAME	HOSPITAL NUMBER	AGE	SEX	LITERACY	OCCUPATION	OP COMPOUND	LETHALITY	EXPOSURE	INTERVAL (hrs)	INTERVAL hrs	QUANTITY	INGESTED WITH	PAST H/O	SMOKING	ALCOHOL	CHOLINERGIC SYMPTOMS	INTENTIONALITY	GCS	P. S. S	APACHE III SCORE	PMR	ACTUAL ICU LOS	RBS	S. AMYLASE	ABG	CPK	TROPONIN T	CKMB	ECG	PCHE DAY 1	PCHE DAY 3	PCHE DAY 5	PCHE DAY 7	ATROPINE DURATION	INTUBATED	DAY OF INTUBATION	DURATION OF VENTILATION	ICU LOS	HOSPITAL LOS	OUTCOME	DISCHARGE DESTINATION
1	MUNIYAPPA	674614	40	M	NIL	LABOURER	PHORATE 10%	EXTREMELY HAZARDOUS	INGESTION	7:00	> 5	< 50 ML	ALCOHOL	NIL	YES	YES	YES	SUICIDAL	E2 V1 M5	MODERATE	64	3.8	4	204	28	MIXED RESP ALK + MET ACID	1045	NEGA	33	OCCA ATRIAL ECTOPICS	2129	1975	3425	4672	4	NO			5	8	RECOVERY	HOME
2	SUSHEELA	675678	30	F	ILLITERATE	SERICULTURE	PHORATE 10%	EXTREMELY HAZARDOUS	INGESTION	4:00	4 - 5	100 ML	RAW	NIL	NO	NO	YES	SUICIDAL	E4 V5 M6	MINOR	26	0.4	4	91	37	MIXED RESP ALK + MET ACID	102	NEGA	21	RAD, NSR	5650	4792	3765	5712	4	NO			5	12	RECOVERY	HOME
3	SHOUIB AHMED	676526	19	M	LITERATE	STUDENT	CHLORPYRIPHOS	MODERATELY HAZARDOUS	INGESTION	4:10	4 -5	100 ML	RAW	NIL	NO	NO	NO	SUICIDAL	E3 V4 M6	MINOR	56	1.3	4	96	50	MIXED RESP ALK + MET ACID	201	NEGA	29	NSR	2434	2319	3468	6721	6	NO			7	11	RECOVERY	HOME
4	MURALI	676899	30	M	LITERATE	GOVT EMPLOYEE	DIMETHOATE	MODERATELY HAZARDOUS	INGESTION	4:10	4 - 5	100 ML	RAW	NIL	NO	NO	YES	SUICIDAL	E4 V5 M6	MODERATE	32	0.5	3	139	22	MIXED RESP ALK + MET ACID	206	NEGA	30	RBBB, S. TACHY	2973	2765	3792	5612	3	NO			4	8	RECOVERY	HOME
5	HARISH	680697	22	M	ILLITERATE	AGRICULTURE	CHLORPYRIPHOS	MODERATELY HAZARDOUS	INGESTION	0:15	< 1	< 50 ML	RAW	CHR DEP RSN	NO	NO	YES	SUICIDAL	E4 V5 M6	MINOR	31	0.4	3	72	52	A/C UNCOMP R AC + M-AC	146	NEGA	16	NSR	5183	4883	5172	6436	4	NO			4	6	RECOVERY	HOME
6	SUDARSHAN	682113	21	M	LITERATE	STUDENT	CHLORPYRIPHOS	MODERATELY HAZARDOUS	INGESTION	4:00	4 - 5	< 50 ML	RAW	NIL	NO	NO	YES	SUICIDAL	E4 V5 M6	MINOR	49	0.9	8	175	62	METABOLIC ACIDOSIS	199	NEGA	33	NSR	200	373	200	246	9	NO			9	14	RECOVERY	HOME
7	MANJUNATH	683377	28	M	LITERATE	SELF EMPLOYED	CHLORPYRIPHOS	MODERATELY HAZARDOUS	INGESTION	4:15	4 - 5	100 ML	RAW	NIL	NO	NO	YES	SUICIDAL	E4 V4 M6	MODERATE	23	0.4	2	112	86	METABOLIC ACIDOSIS	150	NEGA	40	S. TACHY	360	460	212	4632	6	NO			2	9	RECOVERY	HOME
8	ANAND	682671	35	M	ILLITERATE	AGRICULTURE	METHYL PARATHION	EXTREMELY HAZARDOUS	INGESTION	3:30	3 -4	100 ML	ALCOHOL	OLD POLIO	YES	YES	YES	SUICIDAL	E3 V4 M5	SEVERE	58	3.1	6	133	64	A/C R-AC + M-AC	146	POSI	200	NSR	480	300	200	320	7	YES	1	3	8	16	RECOVERY	HOME
9	SUJATHA	684342	26	F	LITERATE	AGRICULTURE	CHLORPYRIPHOS	MODERATELY HAZARDOUS	INGESTION	2:30	2 -3	< 50 ML	RAW	NIL	NO	NO	NO	SUICIDAL	E4 V5 M6	MINOR	35	0.6	6	108	209	MIXED RESP ALK + MET ACID	143	NEGA	29	NSR	200	200	200	204	4	NO			7	12	RECOVERY	HOME
10	THYAGARAJ	684420	28	M	LITERATE	SELF EMPLOYED	QUINALAPHOS	MODERATELY HAZARDOUS	INGESTION	2:30	2 -3	< 50 ML	RAW	NIL	NO	NO	YES	SUICIDAL	E3 V4 M5	MINOR	47	1.3	5	80	59	NORMAL ABG	767	POSI	35	S. TACHY	823	1650	2370	3900	5	NO			6	9	RECOVERY	HOME
11	DHANA KRISHNA	687204	21	M	LITERATE	SELF EMPLOYED	DIMETHOATE	MODERATELY HAZARDOUS	INGESTION	2:45	2 -3	100 ML	RAW	NIL	NO	NO	YES	SUICIDAL	E3 V4 M6	MODERATE	36	0.6	3	89	264	MIXED RESP ALK + MET ACID	423	NEGA	16	LAD, S. TACHY	2620	2125	4972	6232	3	NO			4	8	RECOVERY	HOME
12	RAJENDRA	690188	18	M	ILLITERATE	MASONRY	QUINALAPHOS	MODERATELY HAZARDOUS	INGESTION	2:00	2 -3	100 ML	WATER	NIL	NO	NO	YES	SUICIDAL	E4 V5 M6	MODERATE	31	0.4	7	106	78	MIXED RESP ALK + MET ACID	135	NEGA	20	NSR	370	1307	3084	6125	5	NO			8	11	RECOVERY	HOME
13	SARASAMMA	690477	30	F	ILLITERATE	LABOURER	CHLORPYRIPHOS	MODERATELY HAZARDOUS	INGESTION	0:45	< 1	< 50 ML	WATER	NIL	NO	NO	YES	SUICIDAL	E4 V5 M6	MINOR	32	0.6	9	61	34	METABOLIC ACIDOSIS	159	NEGA	16	NSR	200	862	1548	1885	4	NO			10	14	RECOVERY	HOME
14	NAZIYA	691431	25	F	ILLITERATE	LABOURER	CHLORPYRIPHOS	MODERATELY HAZARDOUS	INGESTION	5:00	> 5	< 50 ML	RAW	NIL	NO	NO	YES	SUICIDAL	E4 V5 M6	MODERATE	44	0.9	5	95	118	MIXED RESP ALK + MET ACID	54	NEGA	60	NSR	1775	1920	2362	4952	7	NO			6	8	RECOVERY	HOME
15	NAGARAJ	691426	25	M	LITERATE	SELF EMPLOYED	PHORATE 10%	EXTREMELY HAZARDOUS	INGESTION	2:00	2 -3	100 ML	ALCOHOL	NIL	YES	YES	NO	SUICIDAL	E4 V5 M6	MINOR	37	0.6	6	89	42	MIXED RESP ALK + MET ACID	141	NEGA	28	NSR	1425	1543	1534	2434	7	NO			7	9	RECOVERY	HOME
16	GOPALA REDDY	699194	48	M	ILLITERATE	FARMER	QUINALAPHOS	MODERATELY HAZARDOUS	INGESTION	1:20	1 -2	< 50 ML	RAW	NIL	NO	NO	YES	SUICIDAL	E4 V5 M6	SEVERE	53	2.7	5	96	110	METABOLIC ACIDOSIS	400	NEGA	46	S. TACHY	261	321	647	1372	5	YES	1	3	6	10	RECOVERY	HOME
17	SUNIL	698857	23	M	LITERATE	STUDENT	CHLORPYRIPHOS	MODERATELY HAZARDOUS	INGESTION	4:00	4 - 5	100 ML	RAW	NIL	NO	NO	NO	SUICIDAL	E4 V5 M6	MINOR	43	0.8	7	52	55	MIXED RESP ALK + MET ACID	891	NEGA	46	S. TACHY	128	1414	1596	2322	8	NO			8	9	RECOVERY	HOME
18	MANI	699657	25	M	ILLITERATE	DRIVER	CHLORPYRIPHOS	MODERATELY HAZARDOUS	INGESTION	3:30	3 -4	< 50 ML	WATER	NIL	NO	NO	YES	SUICIDAL	E4 V5 M6	MINOR	35	0.6	5	158	79	CHRONIC RESP ALK	133	NEGA	35	NSR	1276	1343	1562	2042	5	NO			6	10	RECOVERY	HOME
19	SUVAS	703121	22	M	LITERATE	STUDENT	DIMETHOATE	MODERATELY HAZARDOUS	INGESTION	4:00	4 - 5	< 50 ML	RAW	NIL	NO	NO	YES	SUICIDAL	E3 V4 M6	MINOR	35	0.6	5	96	80	METABOLIC ACIDOSIS	122	NEGA	24	NSR	648	1062	1343	1864	6	NO			6	7	RECOVERY	HOME
20	LAKSHMIAH	703118	60	M	ILLITERATE	LABOURER	CHLORPYRIPHOS	MODERATELY HAZARDOUS	INGESTION	3:40	3 - 4	< 50 ML	RAW	NIL	NO	YES	YES	SUICIDAL	E4 V5 M6	MODERATE	37	0.7	4	89	62	A/C UNCOMP R ALK + M-AC	210	POSI	92	NSR	2495	3693	4162	6048	8	YES	2	3	5	11	RECOVERY	HOME

MASTER CHART

SL NO	NAME	HOSPITAL NUMBER	AGE	SEX	LITERACY	OCCUPATION	OP COMPOUND	LETHALITY	EXPOSURE	INTERVAL (hrs)	INTERVAL hrs	QUANTITY	INGESTED WITH	PAST H/O	SMOKING	ALCOHOL	CHOLINERGIC SYMPTOMS	INTENTIONALITY	GCS	P. S. S	APACHE III SCORE	PMR	ACTUAL ICU LOS	RBS	S. AMYLASE	ABG	CPK	TROPONIN T	CKMB	ECG	PCHE DAY 1	PCHE DAY 3	PCHE DAY 5	PCHE DAY 7	ATROPINE DURATION	INTUBATED	DAY OF INTUBATION	DURATION OF VENTILATION	ICU LOS	HOSPITAL LOS	OUTCOME	DISCHARGE DESTINATION
21	KADIRAPPA	703179	50	M	ILLITERATE	FARMER	METHYL PARATHION	EXTREMELY HAZARDOUS	INGESTION	4:50	4 - 5	100 ML	RAW	NIL	NO	NO	NO	SUICIDAL	E2 V3 M3	MODERATE	88	12	6	155	110	RESP ACIDOSIS	207	POSI	147	S. TACHY	200	218	373	427	8	YES	1	8	8	8	COMPLICATIONS	HOME
22	SHAILA	703501	17	F	LITERATE	STUDENT	CHLORPYRIPHOS	MODERATELY HAZARDOUS	INGESTION	2:45	2 -3	< 50 ML	RAW	NIL	NO	NO	NO	SUICIDAL	E3 V5 M6	MINOR	31	0.4	6	67	50	METABOLIC ACIDOSIS	97	NEGA	10	S. TACHY	200	200	1076	200	8	NO			7	10	RECOVERY	HOME
23	SHOBA	704980	19	F	ILLITERATE	HOUSEWIFE	PHORATE 10%	EXTREMELY HAZARDOUS	INGESTION	4:25	4 - 5	100 ML	RAW	NIL	NO	NO	YES	SUICIDAL	E4 V4 M6	MINOR	47	0.9	7	95	50	METABOLIC ACIDOSIS	159	NEGA	30	S. TACHY	503	1732	3400	5876	8	NO			8	13	RECOVERY	HOME
24	MALASRI	707387	15	F	LITERATE	STUDENT	PHORATE 10%	EXTREMELY HAZARDOUS	INGESTION	2:45	2 -3	100 ML	RAW	NIL	NO	NO	YES	SUICIDAL	E4 V5 M6	MODERATE	44	0.7	3	154	74	METABOLIC ACIDOSIS	137	POSI	136	S. TACHY	326	1599	2672	4214	4	NO			4	7	RECOVERY	HOME
25	BHAGYAMMA	724611	20	F	ILLITERATE	LABOURER	MONOCROTOPHOS	HIGHLY HAZARDOUS	INGESTION	1:00	> 5	< 50 ML	RAW	NIL	NO	NO	YES	SUICIDAL	E2V4M4	MINOR	45	1.1	4	179	94	A/C UNCOMP RESP ALKALOSIS	162	NEGA	26	S. TACHY	200	362	499	1357	7	NO			5	9	RECOVERY	HOME
26	MANJUNATH	694206	20	M	LITERATE	DRIVER	CHLORPYRIPHOS	MODERATELY HAZARDOUS	INGESTION	1:45	1 - 2	50 ML	RAW	NIL	NO	NO	YES	SUICIDAL	E4 V5 M6	MODERATE	41	0.8	7	32	42	MIXED RESP ALK + MET ACID	1470	NEGA	92	NSR	1581	1586	2806	2672	8	NO			8	11	RECOVERY	HOME
27	NARENDRA	709610	22	M	LITERATE	SELF EMPLOYED	PHORATE 10%	EXTREMELY HAZARDOUS	INGESTION	2:00	1 - 2	100 ML	ALCOHOL	NIL	NO	YES	YES	SUICIDAL	E3 V1 M5	MODERATE	44	1	5	244	58	METABOLIC ACIDOSIS	124	NEGA	23	NSR	4216	4654	6068	6142	5	NO			6	8	RECOVERY	HOME
28	SHANTAMMA	725283	25	F	ILLITERATE	AGRICULTURE	CHLORPYRIPHOS	MODERATELY HAZARDOUS	INGESTION	4:45	4 - 5	< 50 ML	RAW	NIL	NO	NO	NO	SUICIDAL	E4 V5 M6	MINOR	44	0.9	3	80	42	CHRO RESP ALK	445	NEGA	14	NSR	6576	8974	7967	8776	6	NO			4	8	RECOVERY	HOME
29	CHOWDAPPA	725617	55	M	ILLITERATE	FARMER	METHYL PARATHION	EXTREMELY HAZARDOUS	INGESTION	2:10	2 -3	< 50 ML	ALCOHOL	NIL	NO	YES	NO	SUICIDAL	E4 V5 M6	MINOR	35	0.8	2	60	209	METABOLIC ACIDOSIS	303	NEGA	40	NSR	4450	5776	6271	7466	4	NO			3	9	RECOVERY	HOME
30	MAMATHA	731658	32	F	ILLITERATE	HOUSEWIFE	PHORATE 10%	EXTREMELY HAZARDOUS	INGESTION	3:40	3 - 4	100 ML	RAW	NIL	NO	NO	YES	SUICIDAL	E3 V4 M5	MODERATE	66	4	5	132	133	METABOLIC ACIDOSIS	561	NEGA	34	NSR	200	672	1274	1896	7	YES	1	1	7	8	RECOVERY	HOME
31	NARAYANA SWAMY	732067	22	M	ILLITERATE	DRIVER	CHLORPYRIPHOS	MODERATELY HAZARDOUS	INGESTION	2:30	2 -3	< 50 ML	RAW	NIL	NO	NO	NO	SUICIDAL	E4 V5 M6	NONE	27	0.3	4	93	75	METABOLIC ACIDOSIS	57	NEGA	73	NSR	200	698	1374	3871	4	NO			5	9	RECOVERY	HOME
32	VASANTHA	732523	25	F	ILLITERATE	HOUSEWIFE	PHORATE 10%	EXTREMELY HAZARDOUS	INGESTION	6:55	> 5	< 50 ML	RAW	NIL	NO	NO	NO	SUICIDAL	E4 V5 M6	MODERATE	65	2.8	3	247	73	METABOLIC ACIDOSIS	502	NEGA	31	S. TACHY	200	409	378	-	3	YES	1	1	3	5	RECOVERY	HOME
33	SURESH H V	733806	40	M	LITERATE	AGRICULTURE	QUINALAPHOS	MODERATELY HAZARDOUS	INGESTION	10:15	> 5	< 50 ML	ALCOHOL	NIL	YES	YES	YES	SUICIDAL	E2 V2 M1	SEVERE	70	7.1	15	82	49	NORMAL ABG	194	NEGA	34	S. TACHY	200	275	403	376	10	YES	1	6	16	21	RECOVERY	HOME
34	NETHRAVATHI	736790	26	F	LITERATE	AGRICULTURE	CHLORPYRIPHOS	MODERATELY HAZARDOUS	INGESTION	8:14	> 5	< 50 ML	RAW	NIL	NO	NO	NO	SUICIDAL	E4 V4 M6	MINOR	38	0.7	1	76	155	CHRO RESP ALK	1149	NEGA	47	NSR	5799	4432	2264	-	3	NO			4	5	RECOVERY	HOME
35	NAVEEN KUMAR	742127	23	M	LITERATE	STUDENT	PHORATE 10%	EXTREMELY HAZARDOUS	INGESTION	1:00	1 - 2	100 ML	RAW	NIL	NO	NO	NO	SUICIDAL	E4 V5 M6	MINOR	38	0.6	9	92	50	METABOLIC ACIDOSIS	365	NEGA	27	NSR	1021	220	260	278	3	NO			3	3	RECOVERY	HOME
36	VENKATESH	716295	25	M	ILLITERATE	FARMER	CHLORPYRIPHOS	MODERATELY HAZARDOUS	INGESTION	2:00	2 -3	50 - 100 ml	RAW	NIL	NO	NO	YES	SUICIDAL	E4 V4 M6	MINOR	42	0.9	6	159	60	ACUTE RESP ACID	46	NEGA	34	NSR	200	203	254	260	1	NO			1	1	RECOVERY	HOME
37	SATISH	768584	30	M	LITERATE	SELF EMPLOYED	CHLORPYRIPHOS	MODERATELY HAZARDOUS	INGESTION	2:00	1 - 2	100	RAW	DEP RSN	NO	NO	YES	SUICIDAL	E3 V4 M5	MODERATE	53	1.6	12	94	143	ACUTE RESP ALK	277	NEGA	19	NSR	477	465	406	319	13	NO			13	44	COMPLICATIONS	HOME
38	ELIYAZ	768581	24	M	ILLITERATE	DRIVER	MONOCROTOPHOS	HIGHLY HAZARDOUS	INGESTION	4:00	4 - 5	< 50 ML	RAW	NIL	NO	NO	YES	SUICIDAL	E3 V5 M5	MODERATE	32	0.5	5	69	192	MIXED RESP ALK + MET ACID	96	NEGA	28	NSR	3496	450	4481	5062	5	NO			7	11	RECOVERY	HOME
39	VENKATESH	768582	28	M	LITERATE	AGRICULTURE	CHLORPYRIPHOS	MODERATELY HAZARDOUS	INGESTION	3:30	3 - 4	100 ML	RAW	NIL	NO	NO	NO	SUICIDAL	E4 V5 M6	MODERATE	59	1.7	4	82	140	METABOLIC ACIDOSIS	122	NEGA	22	S. TACHY	13000	11000	10923	8278	5	NO			4	7	RECOVERY	HOME
40	NAVEEN	767211	18	M	LITERATE	STUDENT	CHLORPYRIPHOS	MODERATELY HAZARDOUS	INGESTION	4:00	4 - 5	50 - 100 ml	RAW	NIL	NO	NO	YES	SUICIDAL	E4 V5 M6	MODERATE	24	0.3	4	64	101	ACUTE RESP ALK	856	NEGA	28	NSR	1103	1409	2402	2510	5	NO			5	7	RECOVERY	HOME

MASTER CHART

SL NO	NAME	HOSPITAL NUMBER	AGE	SEX	LITERACY	OCCUPATION	OP COMPOUND	LETHALITY	EXPOSURE	INTERVAL (hrs)	INTERVAL hrs	QUANTITY	INGESTED WITH	PAST H/O	SMOKING	ALCOHOL	CHOLINERGIC SYMPTOMS	INTENTIONALITY	GCS	P. S. S	APACHE III SCORE	PMR	ACTUAL ICU LOS	RBS	S. AMYLASE	ABG	CPK	TROPONIN T	CKMB	ECG	PCHE DAY 1	PCHE DAY 3	PCHE DAY 5	PCHE DAY 7	ATROPINE DURATION	INTUBATED	DAY OF INTUBATION	DURATION OF VENTILATION	ICU LOS	HOSPITAL LOS	OUTCOME	DISCHARGE DESTINATION
41	SAVITHRAMMA	766894	50	F	ILLITERATE	HOUSEWIFE	CHLORPYRIPHOS	MODERATELY HAZARDOUS	INGESTION	6:45	> 5	< 50 ML	RAW	NIL	NO	NO	NO	SUICIDAL	E4 V5 M6	MINOR	44	1.3	5	86	65	MIXED RESP ALK + MET ACID	242	NEGA	19	S. TACHY	381	298	317	320	6	NO			5	9	RECOVERY	HOME
42	SAKAMMA	772034	18	F	LITERATE	STUDENT	CHLORPYRIPHOS	MODERATELY HAZARDOUS	INGESTION	1:52	1 - 2	100 ML	RAW	NIL	NO	NO	YES	SUICIDAL	E4 V5 M6	MINOR	44	0.7	4	88	121	MIXED RESP ALK + MET ACID	202	NEGA	15	NSR	4052	1326	2406	3012	5	NO			5	9	RECOVERY	HOME
43	MUNIYAMMA	772658	65	F	ILLITERATE	HOUSEWIFE	PHORATE 10%	EXTREMELY HAZARDOUS	INGESTION	6:41	> 5	< 50 ML	RAW	NIL	NO	NO	YES	SUICIDAL	E4 V5 M6	MODERATE	63	2.8	5	345	106	MIXED RESP ALK + MET ACID	1600	POSI	126	S. TACHY	7387	6802	7125	7309	6	NO			6	7	RECOVERY	HOME
44	SANTHOSH	744207	27	M	LITERATE	SELF EMPLOYED	MONOCROTOPHOS	HIGHLY HAZARDOUS	INGESTION	4:21	4 - 5	50 - 100 ml	RAW	NIL	NO	NO	YES	SUICIDAL	E1 V1 M1	SEVERE	85	9.7	4	196	127	ACUTE MIXED ACIDOSIS	123	NEGA	44	S. TACHY	219	342	308	462	6	YES	1	4	5	10	RECOVERY	HOME
45	SHRAVANI	773000	21	F	ILLITERATE	HOUSEWIFE	CHLORPYRIPHOS	MODERATELY HAZARDOUS	INGESTION	2:15	2 -3	100	RAW	G2A 1	NO	NO	YES	SUICIDAL	E4 V5 M6	MINOR	28	0.4	3	118	32	METABOLIC ACIDOSIS	284	NEGA	12	NSR	200	362	800	1434	4	NO			4	7	RECOVERY	HOME
46	SHIVAKUMAR	711835	20	M	LITERATE	UNEMPLOYED	PHORATE 10%	EXTREMELY HAZARDOUS	INGESTION	2:30	2 -3	< 50 ML	RAW	NIL	NO	NO	NO	SUICIDAL	E3 V4M4	NONE	49	1.1	3	159	90	METABOLIC ACIDOSIS	190	NEGA	16	NSR	200	327	318	426	4	NO			4	11	RECOVERY	HOME
47	MD RAHIM	710511	33	M	LITERATE	BUSINESSMAN	CHLORPYRIPHOS	MODERATELY HAZARDOUS	INGESTION	5:00	> 5	100	RAW	NIL	NO	NO	YES	SUICIDAL	E2 V3 M5	MODERATE	41	1.3	6	187	46	MIXED RESP ALK + MET ACID	136	POSI	126	S. TACHY	200	940	2462	-	7	YES	3	5	7	7	DEATH	DEATH
48	SRINIVAS	713373	20	M	LITERATE	AGRICULTURE	CHLORPYRIPHOS	MODERATELY HAZARDOUS	INGESTION	3:00	3 - 4	< 50 ML	RAW	NIL	NO	NO	YES	SUICIDAL	E4 V5 M6	MODERATE	32	0.4	4	78	95	ACUTE RESP ALK	165	NEGA	18	NSR	691	1200	486	900	6	NO			5	9	RECOVERY	HOME
49	PAVANA	711817	54	F	LITERATE	STUDENT	DIMETHOATE	MODERATELY HAZARDOUS	INGESTION	1:00	1 - 2	< 50 ML	RAW	NIL	NO	NO	YES	SUICIDAL	E4 V5 M6	MINOR	40	0.7	3	78	38	MIXED RESP ALK + MET ACID	54	NEGA	37	NSR	985	684	1062	1520	5	NO			4	9	RECOVERY	HOME
50	AMARNATH	716254	18	M	LITERATE	AGRICULTURE	CHLORPYRIPHOS	MODERATELY HAZARDOUS	INGESTION	16:00	> 5	< 50 ML	WATER	NIL	NO	NO	YES	SUICIDAL	E4 V5 M6	MINOR	45	0.8	5	299	86	MIXED RESP ALK + MET ACID	837	POSI	83	S. TACHY	299	256	200	460	4	NO			6	10	RECOVERY	HOME
51	NAGARAJU	707658	45	M	LITERATE	AGRICULTURE	CHLORPYRIPHOS	MODERATELY HAZARDOUS	INGESTION	4:00	4 - 5	< 50 ML	ALCOHOL	NIL	NO	YES	YES	SUICIDAL	E4 V4 M6	MODERATE	60	2.3	5	72	60	METABOLIC ACIDOSIS	148	NEGA	27	NSR	6645	4904	4513	4053	6	NO			6	8	RECOVERY	HOME
52	SHIVA SHANKARA	714592	26	M	ILLITERATE	FARMER	PHORATE 10%	EXTREMELY HAZARDOUS	INGESTION	3:00	3 - 4	100	WATER	NIL	YES	YES	YES	SUICIDAL	E4 V5 M6	MINOR	38	0.7	4	136	52	METABOLIC ACIDOSIS	1439	NEGA	27	NSR	447	200	800	1200	6	NO			5	9	RECOVERY	HOME
53	AMAREESHA	715279	27	M	ILLITERATE	AGRICULTURE	METHYL PARATHION	EXTREMELY HAZARDOUS	INGESTION	1:00	1 - 2	< 50 ML	RAW	NIL	YES	YES	YES	SUICIDAL	E2 V3 M3	MODERATE	80	6.6	7	64	146	METABOLIC ACIDOSIS	600	POSI	164	S. TACHY	864	746	1600	4600	8	YES	1	4	8	10	RECOVERY	HOME
54	SHANKARAPPA	715365	35	M	LITERATE	AGRICULTURE	MONOCROTOPHOS	HIGHLY HAZARDOUS	INGESTION	1:00	1 - 2	< 50 ML	RAW	NIL	NO	NO	YES	SUICIDAL	E2 V4 M4	MODERATE	64	3	9	120	42	METABOLIC ACIDOSIS	265	NEGA	100	NSR	476	926	800	3600	10	YES	3	4	10	12	RECOVERY	HOME
55	HAFEEZA	715649	27	F	LITERATE	HOUSEWIFE	CHLORPYRIPHOS	MODERATELY HAZARDOUS	INGESTION	1:00	1 - 2	< 50 ML	RAW	NIL	NO	NO	YES	SUICIDAL	E4 V5 M9	MINOR	15	0.2	4	100	46	METABOLIC ACIDOSIS	463	NEGA	22	NSR	2600	3473	3682	4232	6	NO			6	7	RECOVERY	HOME