BIOCHEMICAL ABNORMALITIES IN OPC POISONING AND ITS PROGNOSTIC SIGNIFICANCE

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&

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TIRUCHIRAPALLI.

THE TAMILNADU DR.M.G.R. MEDICAL UNIVERSITY

CHENNAI

APRIL-2017

BONAFIDE CERTIFICATE

This is to certify that the dissertation entitled "**BIOCHEMICAL ABNORMALITITES IN OPC POISONING AND ITS PROGNOSTIC SIGNIFICANCE**" is a bonafide original work of **Dr. Alen Binny** in partial fulfilment of the requirements of M.D General Medicine [Branch-1] examination of The Tamilnadu Dr.M.G.R Medical University to be held in April 2017.

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DECLARATION

I solemnly declare that the dissertation titled "**BIOCHEMICAL ABNORMALITITES IN OPC POISONING AND ITS PROGNOSTIC SIGNIFICANCE"** is done by me at K.A.P.VISWANATHAM GOVT MEDICAL COLLEGE, TIRUCHIRAPALLI-1 under the guidance and supervision of Prof.Dr.N.K.Senthilnathan, M.D. This dissertation is submitted to The Tamil Nadu Dr. M.G.R. Medical University towards the partial fulfilment of the requirements for the award of M.D Degree [Branch-1] in General Medicine.

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CONTENT

INTRODUCTION

The modern world thrives well on revolution in the agricultural practices that has resulted in a massive thrust in agricultural productivity. One of the most important step in green revolution is pesticides. Pesticides are a class of toxic substances that are intentionally released into the environment for the greater good it does that exceeds their toxicological concerns. In the developing world, Poisoning is a common method of suicide [(1)]. Pesticide poisoning is a major health hazard in the developing world[(2)]. Millions of people are exposed to these dangerous chemicals because of the occupational hazards and also because of unsafe storage practices[(3)]. However it is the deliberate self-poisoning that causes majority of the deaths and a difficult health strategy to manage among health services, especially in Asia. According to World health organisation report, about three million cases of pesticide poisoning occur every year worldwide and most of them are in Asia, among which 50% of them are organophosphate poisoning. The exact rate of OP poisoning in India is not clear because of under reporting and lack of data. India is an agricultural country and OP compounds are used greatly for the agriculture in India. Therefore the access to these harmful pesticide substances is so easy. In many reports from India, rate of suicidal poisoning with Opc ranges from 10 to 43%[(4)]. Among these patients mortality rate is as high as 20 to 70%[(5)]. In developed countries like United Kingdom, the death due to OP compounds relate to only 1%. This is because in developing countries like India the facilities for early diagnosis and treatment are very limited. The morbidity and

mortality in these patients depends on the time lag between the exposure and the onset of management. So it is very important to recognise the whole spectrum of symptoms in OP poisoning. Organophosphorus compounds inhibit acetyl cholinesterase and butyryl cholinesterase enzymes resulting in excess acetyl choline in the neuromuscular junction causing overstimulation at the cholinergic synapses[6]. The symptoms are classified into muscarinic, nicotinic and central depending on the site of the compound over the respective receptors. Urination, lacrimation, emesis, miosis, excessive salivation, bradycardia, diarrhoea, and wheezing are the muscarinic features. Nicotinic features are paresis, fasciculation, tachycardia, and hypertension. Central features includes confusion, anxiety, seizures, ataxia and psychosis[7]. The need for newer biomarkers in relation to OP poisoning started a very long time ago. OP labelled albumin in plasma, blood beta-glucuronidase and paraxonase status were suggested by some scientists to be very reliable marker for both diagnosis of the poisoning and prognosis. But these assays are not available widely and are very costly. In a limited resourced country like India, we need cheap and easily measurable biomarkers. Many studies were conducted regarding this and were shown that Serum cholinesterase can be a useful tool in the diagnosis of OP poisoning. But its role in prognostication is very minimal. A number of recent studies were conducted using parameters like liver enzymes, serum amylase and serum CPK as newer markers and their correlation with severity and prognosis of OP poisoning[8-11]. Our study was conducted to assess parameters like CPK-MB, Serum potassium, Troponin I in correlation with

Serum cholinesterase along with other liver enzymes, and serum amylase to predict the severity and prognosis in OP poisoning patients.

AIMS AND OBJECTIVES

1. TO MEASURE SERUM ACETYLCHOLINESTERASE, SERUM ELECTROLYTES, LIVER ENZYMES, AMYLASE, CPK, CPK-MB, AND TROPONIN I, IN ACUTE ORGANOPHOSPHORUS POISONING
2. TO ANALYSE THE CORRELATION BETWEEN THESE BIOCHEMICAL PARAMETERS AND SERUM ACETYLCHOLINESTERASE LEVELS
3. TO ANALYSE THE VALIDITY OF THESE BIOCHEMICAL PARAMETERS IN PREDICTION OF SEVERITY AND PROGNOSIS IN OP POISONING

MATERIALS AND METHODS

SOURCE OF DATA:

The present Study was done at Mahatma Gandhi Memorial Govt. Hospital attached with K.A.P.V. Govt. Medical College, Tiruchirappalli.

STUDY DESIGN:

Cross-sectional prospective Study

PERIOD OF STUDY

The study was conducted from June 2015 to June 2016.

ETHICS COMMITTEE APPROVAL

Approval was obtained from Institutional ethics committee.

INCLUSION CRITERIA

All the OP poisoning cases confirmed by history, circumstantial evidence of ingestion, admitted in our hospital within 12 hours of ingestion with characteristic clinical findings and basic laboratory investigations were included in the study

EXCLUSION CRITERIA

- Patients with feature of exposure to another compound not relating to OP Poison.
- Patients with mixed poisoning; OP poisoning and any other poison
- Patients who has chronic alcoholism
- Patients with history suggestive of liver disease

- History suggestive of myopathy
- Patients with history of malignancy and autoimmune diseases
- Patients with history of renal disease
- Patients with history of cardiac disease

CONSENT

An informed consent was obtained from all the participants and their relatives wherever necessary.

SAMPLE COLLECTION

When the patient was admitted in our hospital, after obtaining informed consent, about 5ml of blood was collected in plain tube under aseptic precautions. The blood was allowed to clot and serum was separated by centrifugation and used for the analysis of following parameters.

ESTIMATION OF PARAMETERS

The enzyme creatine kinase catalyses the reaction between creatine phosphate and ADP to creatine and ATP. It is estimated in Kinetic mode using International Federation of Clinical Chemistry (IFCC) methodology. The rate of absorbance change at 340 nm is directly proportional to creatine kinase activity. It is done in a Semi-automated analyser Model BTS 350. The normal expected values are Males- 46-171 IU/L, Female- 24-145 IU/L at 37 degree C.

Creatine kinase has 3 isoforms CK-BB, CK-MM, CK-MB. CK-MM is present in skeletal muscle, CK-BB is present in brain and smooth muscle, while CK-MB is present in myocardium. CK MB is estimated using same principle

used to measure CK, IFCC methodology in Semi-automated analyser BTS 350. The normal expected value is <25 IU/L at 37 degree C.

Cholinesterase also known as acetyl-cholinesterase and is found mainly in the nerve endings and the grey matter of brain. It hydrolyses acetylcholine, released at the nerve endings to maintain transmission of impulses. Cholinesterase level in serum is a useful test of liver function and as an indicator of possible insecticide poisoning. During poisoning the level of enzymes decreases as its activity is inhibited. Cholinesterase catalyses the hydrolysis of butyrylthiocholine substrate forming butyrate and thiocholine. The decrease of absorbance is followed at 405 nm and is proportionate to the activity of cholinesterase in the sample. The mode of reaction is kinetic and the slope of reaction is decreasing. The normal reference value for male is 4620-11500 U/L and for female is 3930-10800 U/L.

Alkaline phosphatase at an alkaline pH hydrolyse into p-nitrophenol phosphate into p-nitrophenol & inorganic phosphates. The rate of formation of p-nitrophenol is measured as increase in absorbance and is directly proportional to the ALP activity in the sample. Reference normal value for ALP is 40 – 147 IU/L.

AST is found in all human tissues and is present in large amounts in skeletal muscle tissue, renal, cardiac, and liver. Increased levels are associated with muscular dystrophy, liver diseases or damage, myocardial injury, etc. Reference normal value for AST is 5 – 34 IU/L at 37 degree C.

ALT is found in high concentration in liver and to a lesser extent in skeletal muscle, pancreas, kidney, spleen, heart, and lungs. AST levels are increased generally as a result of primary liver diseases such as cirrhosis, carcinoma, viral or toxic hepatitis and obstructive jaundice. Reference normal value for ALT is 0-40 IU/L at 37 degree C. All these three enzymes AST, ALT, ALP are estimated using IFCC method in kinetic mode.

Alpha amylase occur in the salivary glands, fallopian tubes, and in pancreas. It catalyses the hydrolysis of a 2-chloro-4-nitro-phenol salt into chloronitrophenol. This rate of hydrolysis is measured as an increase in absorbance because of formation of CNP, which is directly proportional to the alpha amylase activity present in the sample. Amylase is estimated by CNPG3 kinetic method. Reference normal value for Amylase is up to 90 IU/L. AST, ALT, Amylase and ALP are estimated in fully automated analyser EM 360.

Troponin I was tested using qualitative detection rapid card test. The cTnI one step troponin I single use kit is a rapid chromatographic immunoassay for the qualitative detection of cardiac Troponin I in the serum, whole blood, or plasma as an aid in the diagnosis of myocardial injury. Troponin I is a protein present in cardiac muscle and has a molecular weight of 22.5kDa. Troponin I is a subunit of three unit complex with Troponin T and Troponin C. When myocardial injury occurs Troponin I is released in blood after 4-6 hours and remains elevated for 6 to 10 days. The minimum detection level with this rapid card test is 0.5ng/ml. The relative sensitivity of this test kit is 98.5% and relative specificity is 98.4%.

During the analysis internal quality checks using Bio-Rad controls periodically. After the biochemical analysis, all the patients were followed till the end point like recovery, respiratory failure, circulatory failure, CNS complications and any other complications.

Statistical Analysis

All the parameters were tabulated. Mean, Standard deviation were analysed using SPSS 20 software. All the biochemical parameters were correlated with serum cholinesterase using intercorrelations. Chi-square test was the test of significance used for qualitative variables to find the association between them. T test was the test of significance used for comparing quantitative variables with qualitative variable. One-way Anova is used as test of significance to assess various parameters with the compound used for poisoning.

REVIEW OF LITERATURE

INTRODUCTION

Organophosphates are being used as pesticides for more than 60 years worldwide. These agents are used less frequently in the past 10 to 20 years because of the development of carbamates [12]. Around the world, an estimated 3,050,000 people are exposed to organophosphate compounds every year. The documented fatalities include 300,000[13] every year. Toxicity usually results from intentional or accidental ingestion, or exposure to agricultural pesticides [14]. Other potential causes of organophosphate or carbamate poisoning include ingestion of cooking oil or contaminated fruit or, or wearing contaminated clothing. India being an agricultural country, Organophosphates are widely used to increase the production of agricultural commodities. It is estimated that 90% of fatal insecticide poisoning occurs in developing countries[15]. Using insecticide compounds as a mean to end life is grouped under nonviolent methods for suicide. Unemployment, failure in examination, social economical, and domestic problems are all increasing creating psychological stress to the victims. Such stress stimulate these people to consume these OP poisons due to its low price, high availability and high toxicity[16]. In our country these compounds hence are most often are misused as suicidal agents. Since 1963 the incidence of OP poisoning is in a steady rise in India.[8] Agents linked to human poisoning include both organophosphate (parathion, profenofos, chlorpyrifos, Malathion, diazinon) and carbamates (methomyl and aldicarb) insecticides. Accidental poisoning may occur due to inhalation while spraying

insecticide for crops, while self-poisoning is always by ingestion to commit suicide. Large scientific studies suggests that Organophosphate exposure is one of the major threat toxicologically that affects both animal and human health because of its various toxicities like endocrine toxicity, immunotoxicity, neurotoxicity, alterations in cellular oxidation and even genotoxicity. For military purposes organophosphorus nerve agents like sarin, tabun were developed in Germany during 1940s, but they were not used. Medical applications of organophosphates and carbamates include treatment of glaucoma, reversal of neuromuscular blockade (neostigmine, pyridostigmine, and edrophonium), Alzheimer disease (donepezil, pyridostigmine, tacrine and echothiophate), and myasthenia gravis.

CHEMISTRY:

Organophosphates includes various types of molecules with a different biological, chemical, and physical properties along with toxicity. Initially organophosphates were introduced as substitutes for the organochlorine insecticides. Organophosphates are compounds of different volatility, insoluble or soluble in water, organic solvents etc. Chemically these compounds are derivatives of phosphinic (H3PO2), phosphoric (H3PO4), and phosphorous (H3PO3) acids. The compound with significant biological effect have the following general formula.

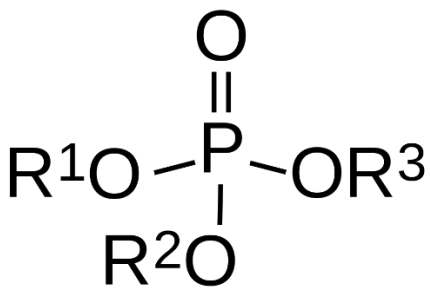


Figure 1 STRUCTURE OF ORGANOPHOSPHATE

Where R1, R2 are hydrogen / alkyl / aryl and others, alkylthio, alkoxy and amino groups. R3 is a removable group, eg: halogens, organic or inorganic acid[17]. Basic characteristics of these compounds is the toxicity profile. Depending on the conditions of its molecular structure, various types (chronic, subchronic, and acute) of toxicity are differentiated. LD50 is used to characterise the acute toxicity.

Toxicity of organophosphates:

Organophosphate toxicity is determined by several factors. Of these, the important ones are the route of contact, molecular structure, and its relation with the biotransformation and detoxification system in the body. Organophosphate compounds are absorbed through inhalation, ingestion, and also through integumentary system. The dissemination of Organophosphates is variable following absorption. The half-life of the compound is short in blood though in some cases it can be several days. OP compounds undergo extensive biotransformation in the body in various organs, by concurrent oxidative biotransformation at various points in the compound, using cytochrome P450 complex. Oxidation is the prime mode of metabolism, also there is cleavage by

esterase, and transfer of the parts of OP compounds to Glutathione. Organophosphate oxidation produces less or more toxic compounds. Following the primary biotransformation process, various conjugation reactions happen resulting in excretion of phosphorus containing residue in urine and faeces. Some residues may remain in the system for a very long time.

CHOLINESTERASES:

Cholinesterase are a group of enzymes that belong to hydrolases dividing the ester bond, to be precise, the esterase subgroup catalysing the hydrolytic reaction of esters to acid plus alcohol. Cholinesterase hydrolyse choline esters readily than other esterase and it is more specific to organophosphates as well as serine. Cholinesterase are subdivided to acetyl cholinesterase and butyryl cholinesterase according to their affinity to their substrates[(18)]. Acetyl cholinesterase or true cholinesterase has more affinity to acetyl-choline comparing to butyryl choline and cleaving acetyl beta methylcholine. The activity of acetyl cholinesterase is high in erythrocytes, the brain and in neuromuscular junction. Excess of substrate will inhibit the acetylcholinesterase enzyme itself. Acetylcholinesterase has different subunits and can be divided into different molecular forms. Butyrylcholinesterase, or pseudo cholinesterase, a nonspecific cholinesterase, is found in pancreas, plasma, and liver and it is synthesised there. Butyrylcholinesterase will not metabolise acetyl beta methyl choline and it has more affinity for butyryl choline and also propionyl choline when comparing to acetyl choline. But

substrate inhibition of cholinesterase is not observed as in acetylcholinesterase. There are Butyrylcholinesterase isoenzymes that are

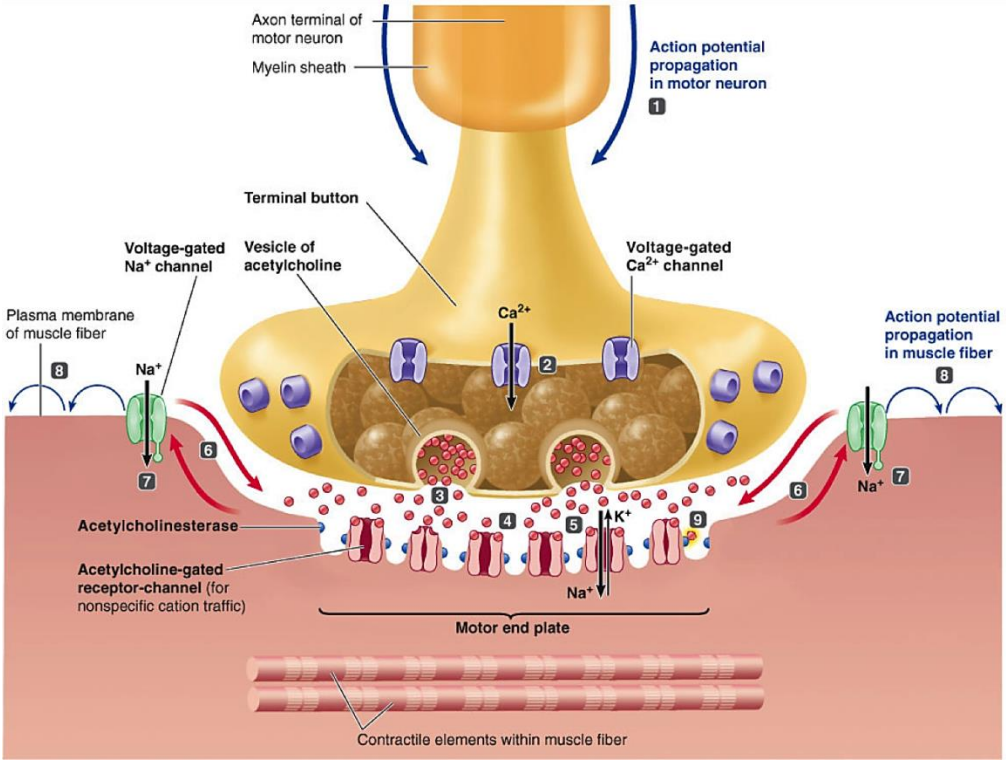


Figure 2 NEUROMUSCULAR JUNCTION

genetically fixed. Based on the genetic setup some persons may have high or low Butyrylcholinesterase activity. Those with genetically reduced Butyrylcholinesterase activity are at an increased risk of cholinergic toxicity when they have exposure to pesticides or succinylcholine[19, 20]. The plasma of persons with standard levels of butyrylcholinestease will bind to Organophosphates/succinylcholine and hydrolyse them and hence the real dose of these penetrating into the tissues will be very low. Both acetylcholinesterase and Butyrylcholinesterase differ not only in their enzymatic property but also in their physiological action[21]. Acetylcholinesterase splits acetylcholine at the neuromuscular junction while butyryl cholinesterase action is involved in

neuromuscular transmission also, it action is in other detoxification processes and lipid metabolism[22].

METABOLISM OF ORGANOPHOSPHORUS COMPOUNDS

ABSORPTION

Organophosphorus compounds contain phosphoric acid derivatives and carbon in their aryl/alkyl groups. These compounds are well absorbed through skin, gastrointestinal tract, and lungs. The extent of absorption rest on the interaction time involved with the integuments, the lipid affinity of the compounds, and presence of organic solvents like toluene/xylene mixed with them, emulsifiers in the preparationthatwillease the absorption. Some other vital factors involved in absorption include volatility of pesticide, porousness of apparel, range of coverage of body surface and personal hygiene of the victim. The degree of absorption also differs as the skin of the area involved varies. E.g., Parathion is easily absorbed into the skin in scrotum, head and neck and axillae, comparing too the skin of arms and hands. The absorption is also high through traumatized integument and existence of dermatitis also permits more absorption of organophosphorus agents[23].

DISTRIBUTION AND STORAGE:

Once Organophosphorus compounds are absorbed, they accumulate in body fat, kidneys, liver, and in salivary glands[24]. Phosphorothioates [P=S] like parathion, diazinon and bromophos has more lipid affinity than the phosphates [P=O] like dichlorvos and hence these are deposited more in body fat and are

responsible for protracted intoxication[25] and relapse after apparent clinical recovery which are observed with these Organophosphate compounds. Organophosphorus compounds are generally lipophilic and hence go through blood-brain barrier more readily in many of the patients[23].

BIOTRANSFORMATION

Phosphates [P=O], they are biologically active inhibitors of acetyl-cholinesterase while Phosphorothioates [P=S] want bio activation to its phosphate metabolite (oxon) to turn active biologically (called *lethal synthesis*)[25, 26]. Hence the toxidrome of Phosphorothioates are late lest aerial oxidation has happened previously to generate the biologically active oxons (more toxic). Organophosphorus agents that are not phosphates are converted to oxon form by oxidation de-sulfuration facilitated by P450 isoforms, in presence of flavin holding monooxygenase enzymes[17].

ELIMINATION

The metabolites of Organophosphorus compounds are eliminated usually through urine and smaller extent in exhaled air and in faeces. The organophosphates which are not stored in fat are excreted in hours however, inhibitory oxons of compounds like chlorpyrifos will remain for days in the body, the reason behind is their depot storage in fat[23].

MECHANISM OF ACTION

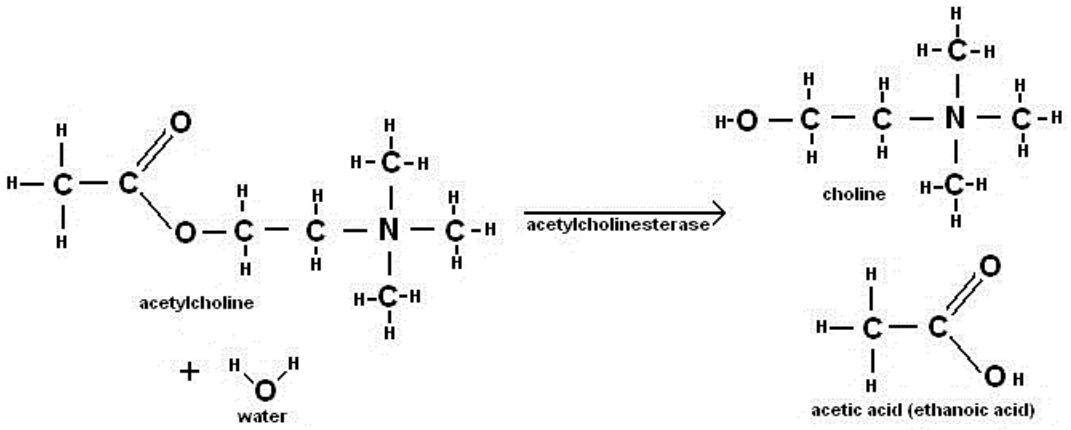


FIGURE 3 ACETYLCHOLINE METABOLISM

Acetylcholinesterase is the enzyme that causes hydrolytic cleavage of acetyl choline to acetic acid and choline. For all pre-ganglionic autonomic fibres and post-ganglionic parasympathetic fibres, acetylcholine is the neurotransmitter. Acetylcholine is also the neurotransmitter at skeletal muscle motor-endplates and inter-neuronal synapses in central nervous system. Action potential transmission is mediated by presynaptic release of acetylcholine in the inter-neuronal cleft. The organization of synapse is in the way that acetylcholine comes in contact with acetylcholinesterase before reaching the postsynaptic receptors, which results in postsynaptic excitatory potential and hence the propagation of action potential. This event is transient because acetylcholine is degraded by acetylcholinesterase. Hence inhibition of acetylcholinesterase causes prolongation of cholinergic post-synaptic transmission time and hence causes continuous cholinergic overstimulation. The Organophosphate agents inhibit the activity of acetylcholinesterase by a catalytic reaction wherein the serine-hydroxyl moiety in the active site

(esteratic site) of the enzyme is phosphorylated [27, 28]. The cleavage of carbon-enzyme bonds in acetylcholine is completed in a very few micro-seconds. But the cleavage of phosphate-enzyme bond needs a long period

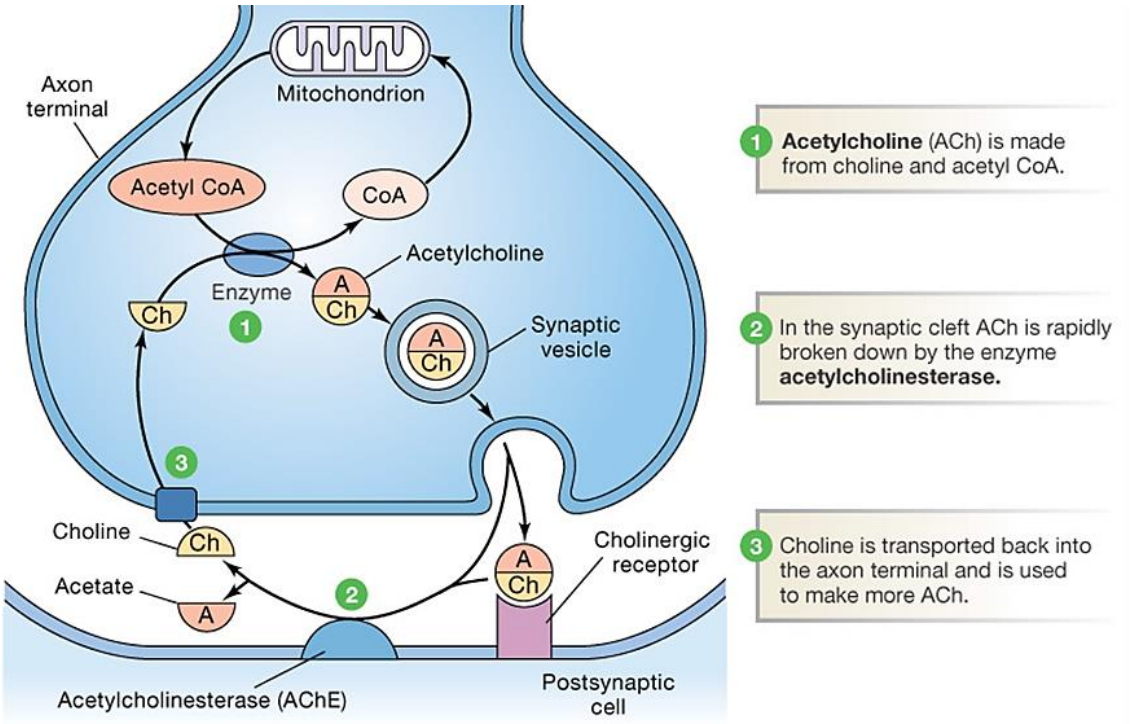


Figure 4 Acetylcholine Metabolism 2

varying from sixty minutes to quite a few weeks depending upon the organophosphate agent involved. Spontaneous reactivation of the phosphorylated enzyme may occur, but the reactivation rate depends on the tissue as well as the prosthetic group which got bound to the enzyme. O-O dimethyl phosphorylated acetylcholinesterase gets reactivated spontaneously in one day which hence assists recovery from the cholinergic crisis. Reactivation of O-O diethyl phosphorylated acetylcholinesterase is considerably sluggish[29][27, 28]. The response to oximes for reactivation of inhibited cholinesterase declines with time because of "*ageing*" of the inhibited acetylcholinesterase. Ageing of the phosphorylated enzyme is most likely due

to loss of one alkoxy or alkyl group, resulting in a more stable compound, monoalkyl- or monoalkoxy-phosphoryl acetylcholinesterase. The rapidity of ageing of acetylcholinesterase is in the order isopropyl-methyl>dimethyl>di isopropyl>diethyl [29].

Delayed neurotoxic effect of Organophosphorus compounds is not because of acetylcholinesterase inhibition, instead it is due to phosphorylation of a particular esteratic enzyme in the neurons[30, 31] called “neurotoxic esterase” or neuropathy target esterase (NTE)[32, 33] . The first catalytic step is phosphorylation of neuropathy target esterase. The next reaction which is the cause for neuropathy is the biotransformation of the phosphorylated-enzyme to an aged compound[34].

Some other enzymes in the body are also phosphorylated including lipases, chymotrypsin, and trypsin by organophosphate compounds. The rate of reaction is slow generally with these enzymes. The clinical effects of inhibition of these enzymes are not known yet[29].

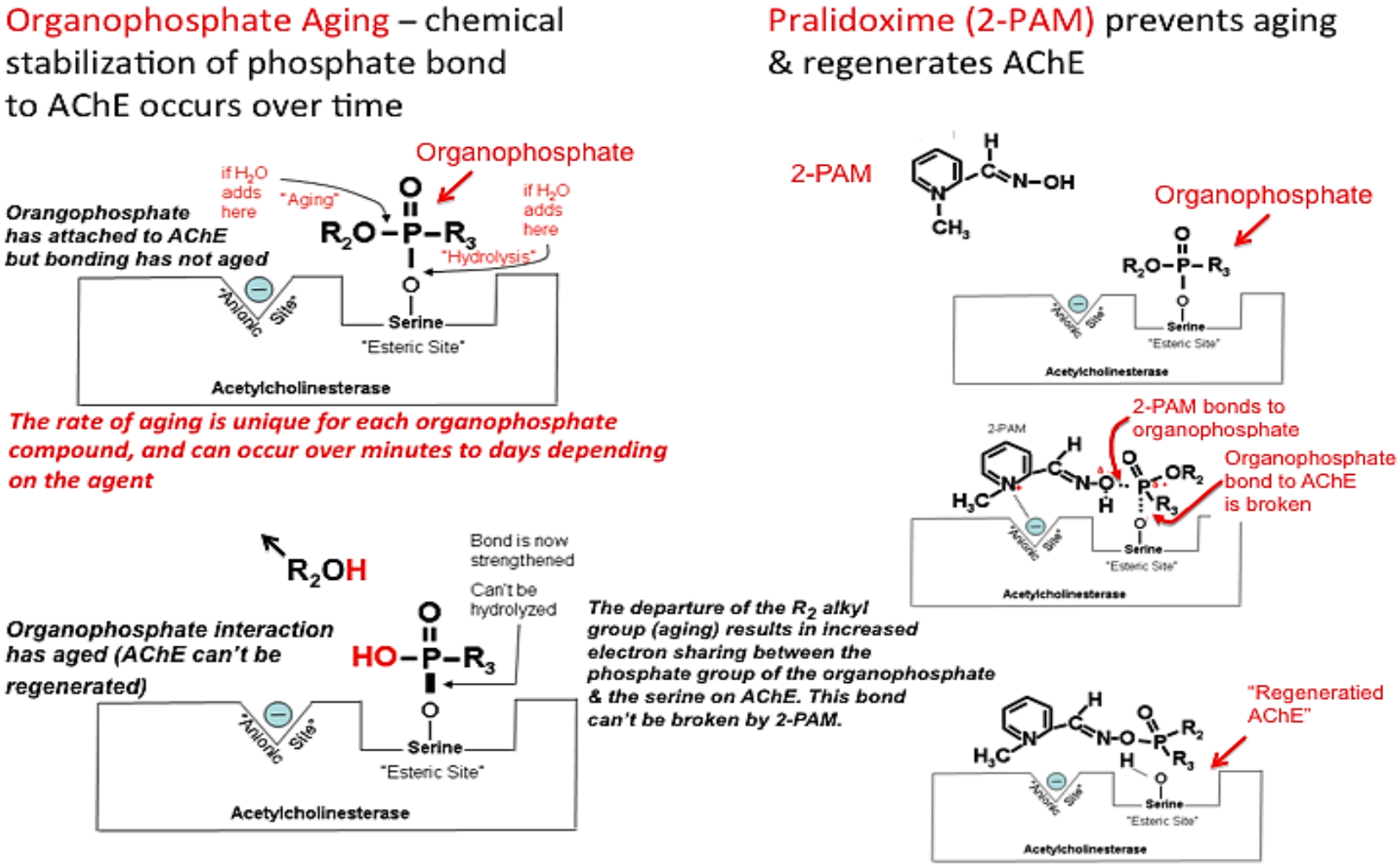


Figure 5 ORGANOPHOSPHATE AGEING

MYOPATHIC EFFECTS

Muscular weakness following organophosphate poisoning was one of the earliest findings discovered by Carey. Necrotic changes is extensive in motor endplates[35]. The maximal necrosis happens during one to three days and recovery features starts at 7th day, and full recovery occurs at two to three weeks. OP induced myopathy is distinct from neuropathy that begins approximately after 3 weeks when normal muscle strength returns[36]. Failure to sustain tetanic stimulation was witnessed following OP poisoning in investigational animals. When normal muscle sustains tetanic stimulation at 25 Hz, 50 Hz, 100 Hz, & 200 Hz for ten seconds, 2-4 hours after organophosphate poisoning, at 100 Hz the contractions were insufficient, and at 200 Hz it was absent. Muscle paresis observed in the OP poisoning patients after an apparent recovery from the acute crisis due to cholinergic activation but before the onset of polyneuropathy is identified as intermediate syndrome[37]. High concentration of acetylcholine at the motor endplates causing prolonged depolarisation is due to prolonged change in ion flux of junctional membrane and it is considered to be the cause of muscle necrosis[38]. The severity of myopathy correlates with the degree and duration of acetylcholinesterase inhibition which initiates a neutrally mediated events, causing increased neurotransmitter release and antidromic activity[39]. Dissolution of the Z bands of sarcoplasmic reticulum suggests disturbances in the Calcium flux following organophosphate poisoning[35].

RESPIRATORY DISORDERS

Organophosphate compounds cause a CNS depression of respiration in animals. The important findings are swiftly advancing bradypnea and resulting in apnea because of reduced respiratory effort. There is evidence to suggest a fall in central inspiratory drive due to OP poisoning[40]. There is also some studies to suggest an intact respiratory muscles activity following OP poisoning but having respiratory failure[41].

HEPATOLOGICAL DISORDERS

The bio-activation and metabolism of Organophosphorus molecules happen in liver. They are excreted chiefly through renal system[42]. The profile of hepatic transaminases, antioxidant-enzymes, and trace elements are very much affected following organophosphate poisoning[43]. The histopathological findings in human liver after an acute OP poisoning are, centrilobular necrosis, congestion, fatty changes, and sinusoidal dilatation[44].

CARDIOVASCULAR DISORDERS

Myocardial necrosis following Organophosphate poisoning was reported by Povoa et al[45]. Elevation in creatinine kinase and lactate dehydrogenase following organophosphate poisoning[46]. Sinus tachycardia, hypertension, sinus bradycardia, hypotension, impaired force of contraction, myocardial necrosis are the cardiac manifestations[47]. Ecg changes are Prolonged QT interval, low amplitude T waves, ectopic beats, ST segment elevation, and PR interval prolongation[48].

NERVOUS SYSTEM DISORDERS

In experimental rats, necrosis of neurons has been demonstrated in sub-cortical and cortical areas following acute large doses of organophosphate poisoning[47]. There are several neurological disorders reported in acute or chronic organophosphate poisoning[23]. These syndromes vary widely, which include parkinsonian signs, pseudo bulbar signs, OP induced delayed peripheral neuropathy, changes in libido, affect and memory, psychiatric and a slowly progressive neuro-psychological disturbances (chronic organophosphate induced neuropsychiatric disorder) and cerebellar syndrome[49].

HORMONAL IMBALANCE

Several adverse outcomes regarding fertility due to sex hormone imbalance because of pesticide exposure has been published in late 20th century including feta death, congenital malformations, and intrauterine growth restriction[50]. Since a large exposure to pesticides occur when living in rural area, it is a potential risk factor for infertility[51].

ESOPHAGEAL EFFECTS

Esophago-gastroscopy immediately following organophosphate poisoning revealed oedema, circumferential hyperaemia, and punctate bleeding throughout the esophagus[23].

RENAL IMPAIRMENT

Many studies and case reports have been documented regarding organophosphate poisoning and the causation of acute renal failure. It is also shown that prolonged exposure to pesticides lead to chronic kidney disease[23]

ANTIOXIDANT STATUS PLUS OXIDATIVE STRESS

Enhanced lipid peroxidation, elevated oxidative stress and reduced glutathione levels have been shown in Organophosphate poisoning[52, 53].

ORGANOPHOSPHATE POISONING AND PREGNANCY

OP poisoning in pregnancy has caused pre natal and post natal death and congenital abnormalities in experimental animals. The congenital abnormalities include, limb defects, polydactyly, hydroureter, vertebral deformities, and cleft palate[29]. During 3rd month of pregnancy, following organophosphate poisoning, the fetus was aborted in one case as continuation of pregnancy was considered harmful[54, 55]. But successful management of OP poisoning during 2nd and 3rd trimester had resulted in term deliveries and normal healthy babies[55].

CLINICAL MANIFESTATIONS

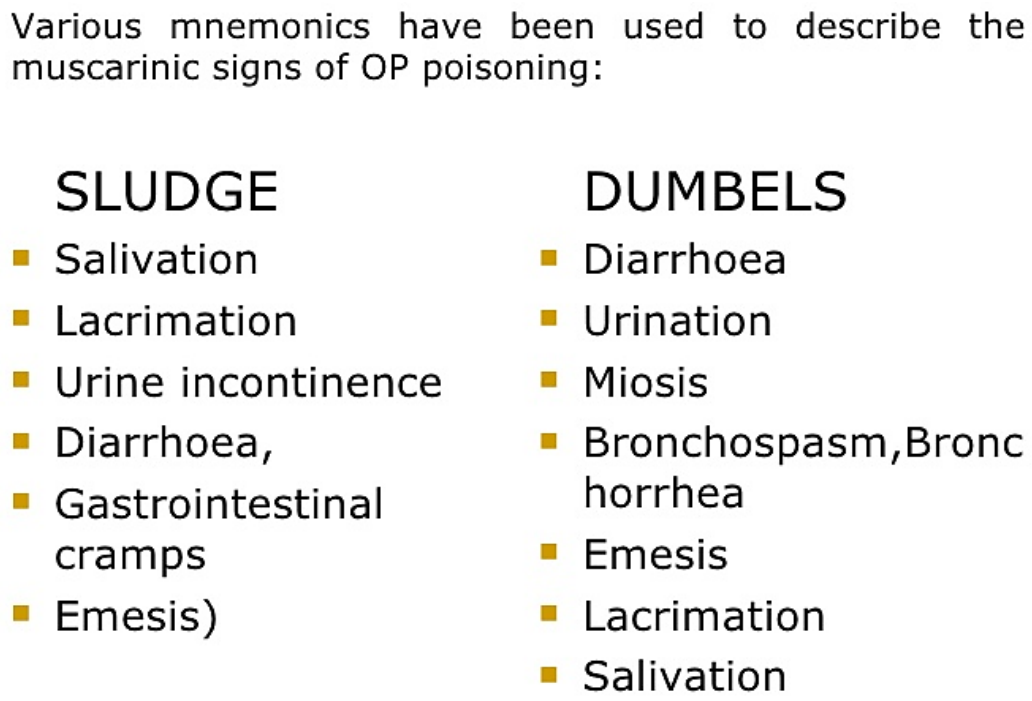


Figure 5 MUSCARINIC SIGNS OF OP POISONING

Cholinergic manifestations can be summarised under three categories namely, muscarinic, nicotinic, and central. The symptoms appear varying in combination. The intensity and onset time of symptoms depends on the mode of poisoning and composition of the poison. When the ingestion is massive then the symptoms arise within minutes. Most of the times the symptoms arise within 30 minutes of exposure and in less than 12 hours. The usual cause of death and the most serious manifestation is respiratory failure which results from paresis of muscles of respiration, central depression of respiratory drive, aggravated with bronchospasm and excessive airway secretions. Impaired consciousness and vomiting also leads to aspiration pneumonitis. Increased

cholinergic activation causes bradycardia and may lead to heart blocks. The `muscarinic signs are easily remembered as SLUDGE/BBB – Salivation, Lacrimation, Urination, Defecation, Gastric emesis, Bronchorrhea, Bronchospasm, and Bradycardia or as DUMBELS – Defecation, Urination, Miosis, Bronchorrhea/Bradycardia, Emesis, Lacrimation, and Salivation [56]. A few case reports suggest that there is signs of myocardial ischemia like elevated troponin or ECG changes in Organophosphorus poisoning [57, 58]. The levels of troponin peaks on presentation in most of the cases and the risk is more in older patients but is very low in mild poisoning.

INTERMEDIATE SYNDROME

The onset is acute in IMS, and is usually manifests 24 to 96 hours after poisoning, affecting the patients who are conscious without cholinergic features or fasciculations. The presentation of this syndrome is paresis affecting preferentially the proximal group of muscles in limbs and flexors of neck[59]. Musculature that are innervated by cranial nerves III to VII and X are also involved in various combinations. This syndrome increases the risk of death, because of the respiratory arrest which unless recognised timely and treated promptly [60]. These patients are usually conscious, and they show marked anxiety, restlessness and sweating because of progressive hypoxia. The most important feature is significant neck muscle weakness and the victims are not able to lift the head from pillows. They also show more weakness in hip flexion and shoulder abduction. These musculature do not have fasciculations and the stretch reflexes are reduced or often absent[61]. No sensory impairment is noted

in intermediate syndrome. Intermediate syndrome is likely to result from the post synaptic neuromuscular dysfunction. The risk factors for this syndrome includes highly fat soluble Organophosphorus agent and also linked to inadequate doses of oximes[62]. It is not usually described in carbamate poisoning. With adequate supportive care, prolonged mechanical ventilation, most people recover completely from this neurological dysfunction within 2 to 3 weeks. Clinical deterioration and improvement correlates with RBC cholinesterase levels.

BOX 1 DIFFERENCES BETWEEN IMS AND OPIDN

	IMS	OPIDN
Time of onset	One to four days	Two to three weeks
Site of weakness	Proximal	Distal
Neck muscles	+	-
Limb muscles	+	-
Cranial nerves	+	-
Ventilatory muscles	+	-
Electromyogram	Tetanic fade	Denervation
Organophosphorus agents	Fenthion Monochrotophos	Methmidophos, Chlorpyrifos
Recovery	4-18 days	6-12 months

DELAYED AND LONG-TERM NEUROPATHOLOGY

IT occurs one to three weeks after ingestion of Organophosphorus agents like chlorpyrifos [63, 64]. Carbamates are very rarely cause development of delayed peripheral neuropathy [65, 66]. The mechanism of causation of delayed neuropathy involves inhibition of neuropathy target esterase NTE rather than RBC cholinesterase [67]. The patients who are affected usually presents with glove and stocking paraesthesia subsequently resulting in symmetrical motor polyneuropathy which manifests by flaccid weakness of lower extremities which may ascend to affect upper extremity. Sensory involvement is usually minimal. Delayed neuropathy usually involves distal group of muscles but in severe poisoning proximal groups may also get involved [68]. Electromyogram and nerve conduction studies show reduced firing of motor conduction units [69]. Histopathological analysis of the involved peripheral nerves show wallerian degeneration of large distal axons [70]

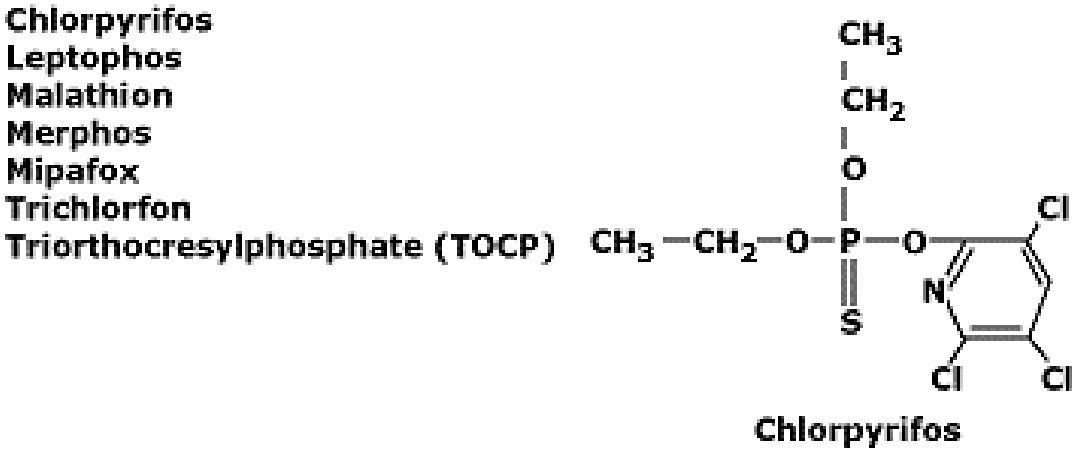


Figure 6 AGENTS ASSOCIATED WITH DELAYED PERIPHERAL NEUROPATHY

DIAGNOSIS

Organophosphate poisoning is usually diagnosed on the basis of clinical scenario. If known ingestion or exposure to OP agent is not evident, the clinical signs of cholinergic crisis may show the likelihood of organophosphate poisoning. Many organophosphate compounds have a characteristic garlic like or petroleum odour which is useful in making the diagnosis. Because of the significant variability in toxicity, effort must be made to precisely identify the agent involved. It is imperative to find out if a dimethyl or diethyl poison is involved. The duration of toxidrome and the therapeutic window during which the treatment with an oxime is likely to be effective are markedly different between these two groups of organophosphate compounds. Dimethyl compounds undergo rapid ageing, hence the therapy with oxime is critical; diethyl compounds exhibits delayed toxicity and hence require a prolonged treatment[13]. Clinical signs of Organophosphorus toxicity express when the cholinesterase values drop to less than 75%. It will be < 10% in clinically overt poisoning [23, 71, 72]. If there is a doubt whether an organophosphate is ingested or not, 1 mg of atropine in adults or 0.01 to 0.02 mg/kg of atropine in children can be tried. Following atropine injection if there is no signs and symptoms of anticholinergic effects then it suggests the diagnosis of poisoning with acetylcholinesterase inhibitor. Bardin's classification is used for grading the patient according to clinical findings[73]

BOX 2 BARDIN'S CLASSIFICATION OF DEGREE OF ORGANOPHOSPHATE POISONING

Bardin's classification of degree of Organophosphate poisoning[73]	
Grade 0	No clinical manifestations
Grade 1	Hyper secretion, fasciculations, Conscious
Grade 2	Grade 1 +unconsciousness, hypotension
Grade 3	Grade 2 + abnormal chest x-ray, Stupor, pO_2less than 10 mm Hg

LABORATORY ABNORMALITIES

Measurement of RBC cholinesterase activity is a measure of level of toxicity. Sequential measurement of cholinesterase levels also helps in assessment of adequacy of oxime therapy in regeneration of cholinesterase levels. Plasma cholinesterase estimation is easily done and hence employed in most of the laboratories but it does not correlate well with the severity of poisoning like RBC cholinesterase[74]. Several liver enzyme abnormalities are noted in OP poisoning including elevations in ALT, AST, and ALP. Serum amylase is also noted to get elevated because of excessive cholinergic stimulation of pancreas. Creatine phosphokinase get elevated in OP poisoning during the acute phase and also during the intermediate syndrome. Few studies have reported elevation in CPK-MB and troponin levels indicating myocardial necrosis in organophosphate poisoning.

MANAGEMENT

Severe organophosphate intoxication is a medical emergency. The management starts with patent airway, breathing, & circulation. O_2 must be provided at the earliest. The victim is kept in left-lateral position along with extended neck. Inorder to keep the airway patent and reduce the risk of aspiration this position is useful. It also slows the gastric transit and hence decreases absorption of the poison[75]. Stomach wash is effective if given within thirty minutes of poisoning, and if it is delayed it can also be done on admission after confirming that the airway is secure. Induction of vomiting with emetics like ipecacuanha must be avoided, because unconsciousness can rapidly set-in before vomiting[76]. In patients with topical exposure there is potential risk for dermal absorption and hence aggressive decontamination, complete removal of contaminated clothes from the body and complete cleansing of the involved parts must be done. Patients' garments and stuffs that are contaminated must be cast-off because it can absorb the OP compounds and re-exposure to patient can occur even after washing. Health care workers should take necessary precautions to avoid accidental exposure to such contaminated clothing and also providing treatment in well ventilated areas [77-79]. Moderate to severely intoxicated patients having depressed sensorium need 100% O_2 and endotracheal intubation for mechanical ventilation. Patients who appear to have mild poisoning may also quickly develop failure of respiration due to nicotinic receptor mediated diaphragmatic weakness, CNS respiratory center depression, bronchospasm and copious secretions. So these patients may

also be considered for an early intubation. Patients with cholinergic toxicity due to organophosphate poisoning are treated with atropine and oxime therapy.

ATROPINE

Atropine acts like a physiological antidote, competes with the acetylcholine at the muscarinic receptors, thus preventing cholinergic activation. In patients with moderate to severe poisoning, atropine is initiated in a dose of 2mg to 5mg intravenously for adults repeated at intervals of 5 to 10 minutes and 0.02 to 0.05mg per kg for pediatric age group & repeated at intervals of 10 to 30 minutes[80]. If there is no improvement the dosage is doubled every 3 to 5 minutes till pulmonary muscarinic signs reduces. There is no need for providing oxygen prior to administration of atropine [81]. The dosing of atropine must be increased or decreased to the point of clearing the airway secretions and relief of Broncho-constriction. Tachycardia and Mydriasis are not markers appropriate for therapeutic improvement, because they may indicate hypovolemia, continued hypoxia, or sympathetic stimulation[82]. Continuous observation is required to ensure maintenance of adequate atropinisation. A heart rate of exceeding 140 beats per minute must be avoided. ST segment changes in Ecg can be caused by large doses of atropine, which can be

Figure 7 ATROPINE SULFATE

reverted with propranolol without the need for reducing the dosage of atropine[83].

OXIMES

Oximes compounds that can re-activate the phosphorylated acetylcholinesterase more quickly than the spontaneous re-activation by hydrolysis. They have three main actions[84]: (1) transforming the OP agent into a non-reactive compound by a direct reaction (2) protecting cholinesterase from sustained inhibition by a transient reaction (3) re-activation of the alkyl-phosphorylated AchE to release the active enzyme. There are plenty of oximes studied to date, but molecules with clinical utility can be subdivided into two classes namely, mono-pyridinium and bis-pyridinium. The only used mono-pyridinium is Pralidoxime (P_2AM) whereas other bis-pyridinium compounds include obidoxime, trimedoxime, and asoxime. There is no universal agreement on which is the most effective oxime and its dosing regimen.

Figure 8 PRALIDOXIME

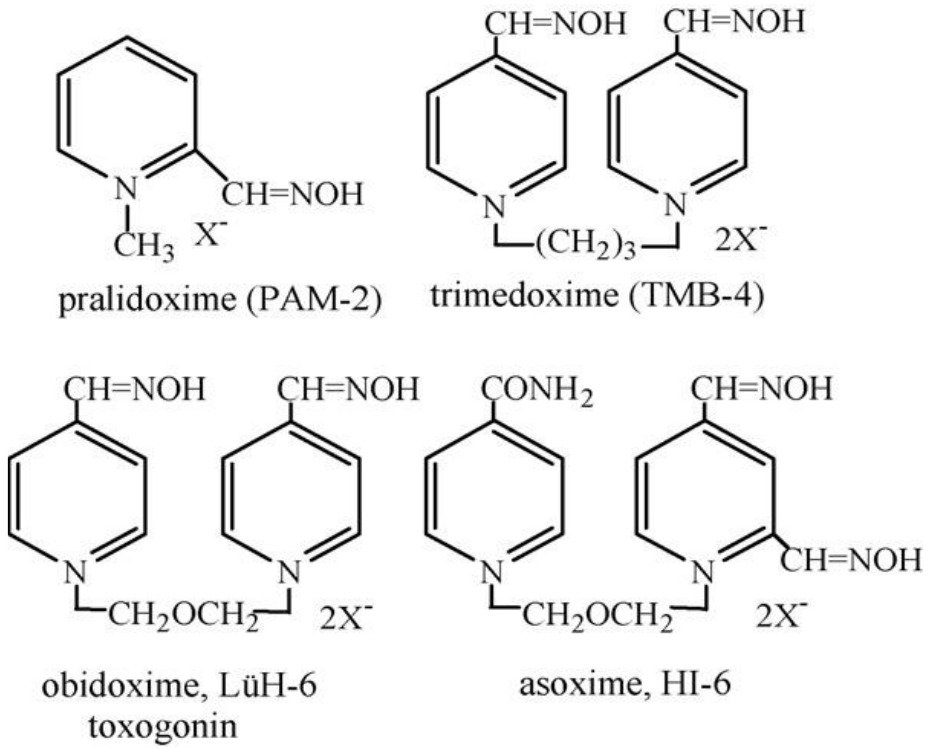


Figure 9 TYPES OF OXIMES

WHO commends that oximes should be administered to those patients who require atropine[85]. Inorder to maintain the therapeutic concentration, a loading-dose should be given at first followed by a continuous infusion of Oximes. The loading-dose must not be administered as a iv bolus because it can cause vomiting (may lead to aspiration), diastolic-hypertension and tachycardia[86]. The bolus dose is given as 2 grams iv followed by 500 mg/ hr as infusion continuously till clinical progress is noted or 30 mg per kg body-weight as bolus iv for 4 to 6 hrs. Or 8 – 10 mg/kg/hr IV till complete recovery. For patients who develop intermediate syndrome, Pralidoxime is given for longer periods till they are weaned off from mechanical ventilation. Pralidoxime may also be given as s.c or i.m. In view of very short elimination half-life 1.2 hours following an IV injection, continuous infusion is found to be

better than bolus therapy to maintain therapeutic concentrations. The maximal recommended dose of Pralidoxime is 12 grams in 24 hours for adults. Huge doses of P_2AM and other oximes themselves can lead to neuro-muscular blockage and inhibition of acetylcholinesterase. Pralidoxime must be given as soon as possible in organophosphate poisoning, atleast within 24-36 hours, for the reason that reactivation of acetylcholinesterase is primarily reliant on life span of RBC when the enzyme ages and thus regeneration may take weeks. P_2AM is not equally efficacious to every organophosphate compound. The effects of diethyl compounds are antagonised more efficiently than that of dimethyl/ dimethoxy-compounds[29].

BENZODIAZEPINES

Organophosphate poisoning patients commonly develop restless delirium. It could be pesticide itself, atropine toxicity, and alcoholic intoxication along with poisoning and other medical complications. Restless patients may improve on treatment with diazepam[87]. Studies done in animals show that diazepam decreases neuronal damage and precludes respiratory failure in OP poisoning however human trials are few[87]. Prophylactic diazepam had shown to reduce the incidence of neurocognitive dysfunction after OP poisoning [88, 89]. There is no evidence that phenytoin has effect on organophosphate compound induced seizures and hence it is not recommended.

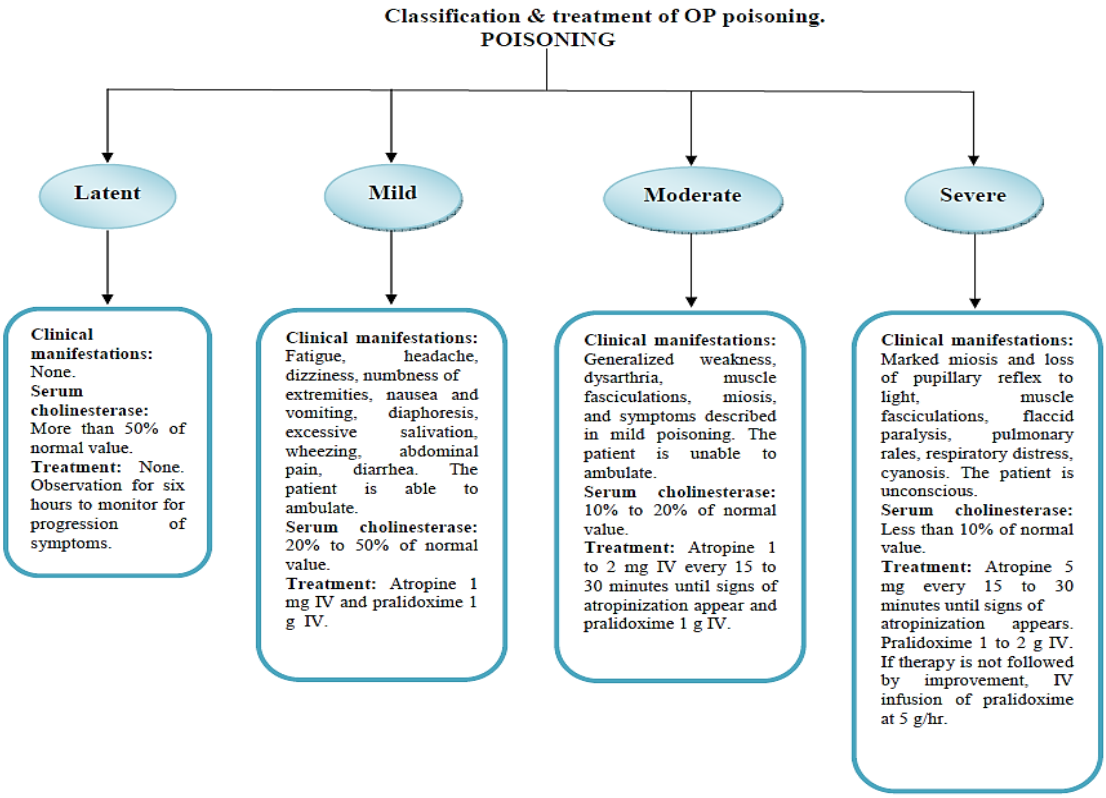


Figure 10 SUMMARY OF OPC POISONING

OTHER THERAPIES UNDER RESEARCH:

Magnesium sulphate acts by blocking ligand-gated calcium channels at the neuro-muscular junction and hence results in deprived acetylcholine release from presynaptic terminals, resulting in improved functioning of neuromuscular junctions and prevents activation of NMDA receptors and overstimulation of CNS.

Sodium bicarbonate is used in Iran and Brazil for treatment of Opc poisoning instead of oximes. Escalation in pH of blood upto 7.45 – 7.55 has resulted in better result in dogs by an unknown mechanism[(90)].

Clonidine is an agonist of alpha 2-adrenergic receptor that reduces acetylcholine synthesis and also its release from pre-synaptic terminals.

Experiments in animals has shown better results when treating with clonidine along with atropine, however the studies in human being are undergoing.

When the organophosphate compound is removed from blood it can allow better action of other treatments. The part of hemofiltration and haemodialysis are not clear in management of OP poisoning. The benefit of hemofiltration has been shown in a research done in China following poisoning with dichlorvos, an OP agent with poor lipid solubility and thus having small volume of distribution.

In a study conducted in China, Fresh frozen plasma was used along with the traditional treatment for OP poisoning. It is observed that for every two bags of FFP given there is an increase of 461.7+/- 1421.1 IU/L in the levels of butyrylcholinestease. Since OP agents may get released from the fat tissue slowly for a prolonged period, FFP doses must be repeated till Butyrylcholinesterase goes up to a desirable level[91].

PON1 (Paraoxonase) is an important enzyme in the metabolism of organophosphate agents. Though hydrolysis PON1 can deactivate certain organophosphate agents. PON1 hydrolyses only the metabolic end-products of the organophosphate agents and not the parent compounds[92]. There are PON1 polymorphisms which causes different individuals to have variable susceptibility to individual OP agents. If the PON1 concentration is higher it offers better protection to the individual. Further data regarding PON1 are under research[93].

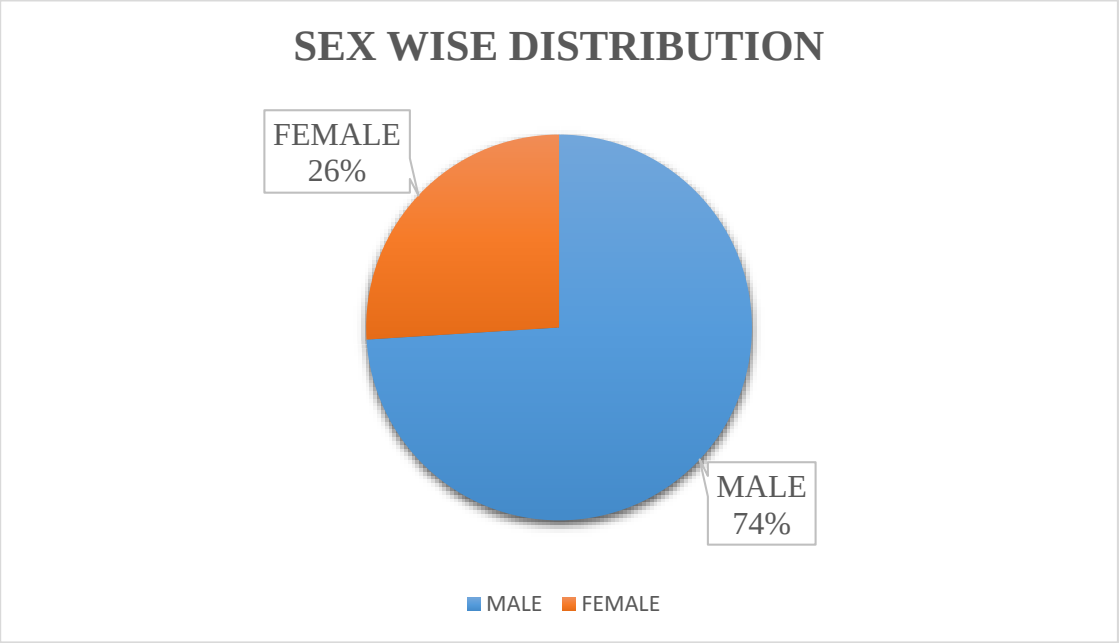
STATISTICS

SEX RATIO

Table 3 SEX RATIO

SEX	No.of respondents (n=50)	Percentage (100%)
Male	37	74.0
Female	13	26.0

In this study with a total participants of 50 patients, 37 of them are male (74%) and 13 of them are female (26%).

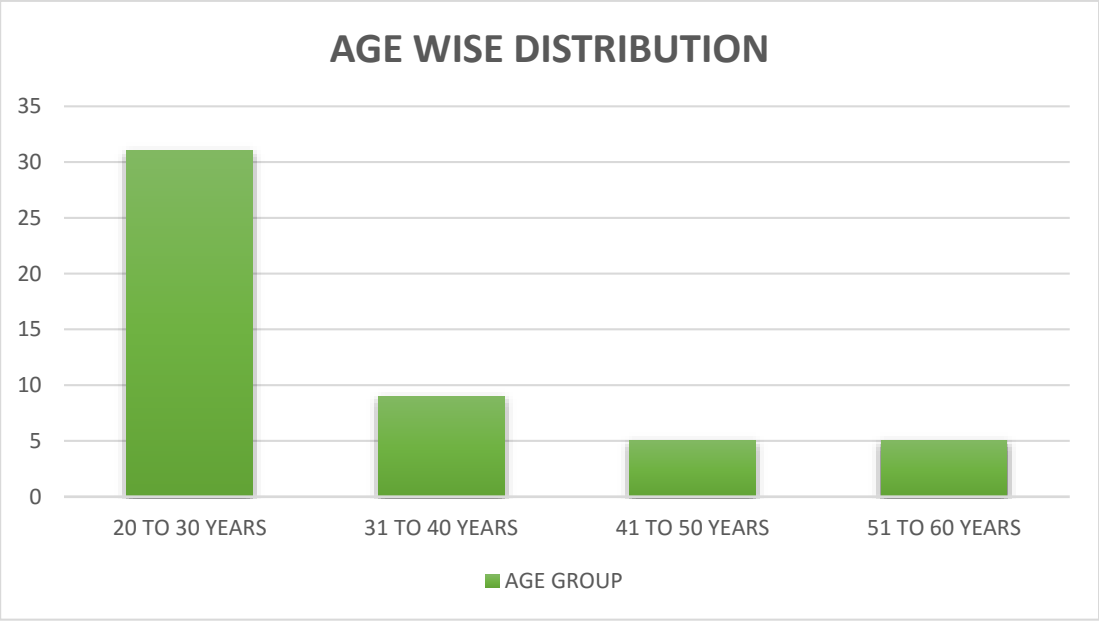


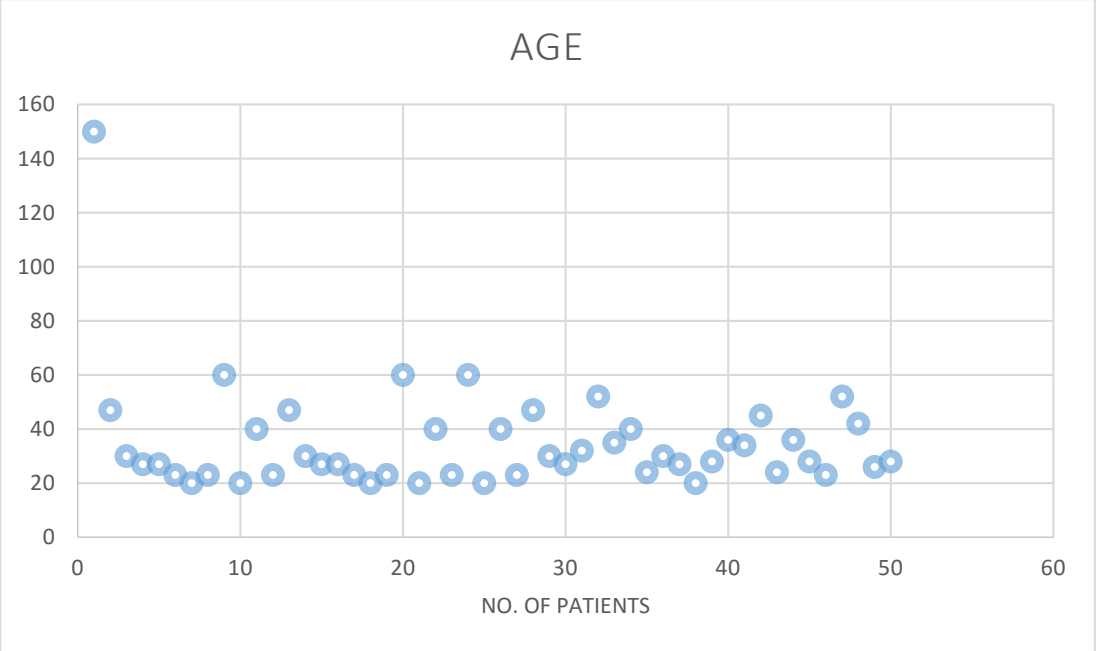
AGE WISE DISTRIBUTION

Table 4 AGE WISE DISTRIBUTION

Age	No.of respondents (n=50)	Percentage (100%)
20 to 30yrs	31	62.0
31 to 40yrs	9	18.0
41 to 50yrs	5	10.0
51 to 60yrs	5	10.0

In this study, the total number of participants include 50 patients, and among them 31 of them (62%) belong to 20 to 30 years age group.





TYPES OF COMPOUND INGESTED

Table 5 TYPES OF COMPOUND INGESTED

COMPOUND	No.of respondents (n=50)	Percentage (100%)
CARBOFURAN 3%	3	6.0
CHLORPYRIFOS 20%	8	16.0
DIMETHOATE 30%	5	10.0
FOLLIDOL	9	18.0
PROFENOFOS 20%	1	2.0
PROFENOFOS 40%	1	2.0
PROFENOFOS 50%	19	38.0
TRIZOPHOS	4	8.0

In this study group the commonest compound ingested is 50% Profenofos (19 patients), followed by Follidol (9 patients), Chlorpyrifos 20% (8 patients), and dimethoate 30% (5 patients).

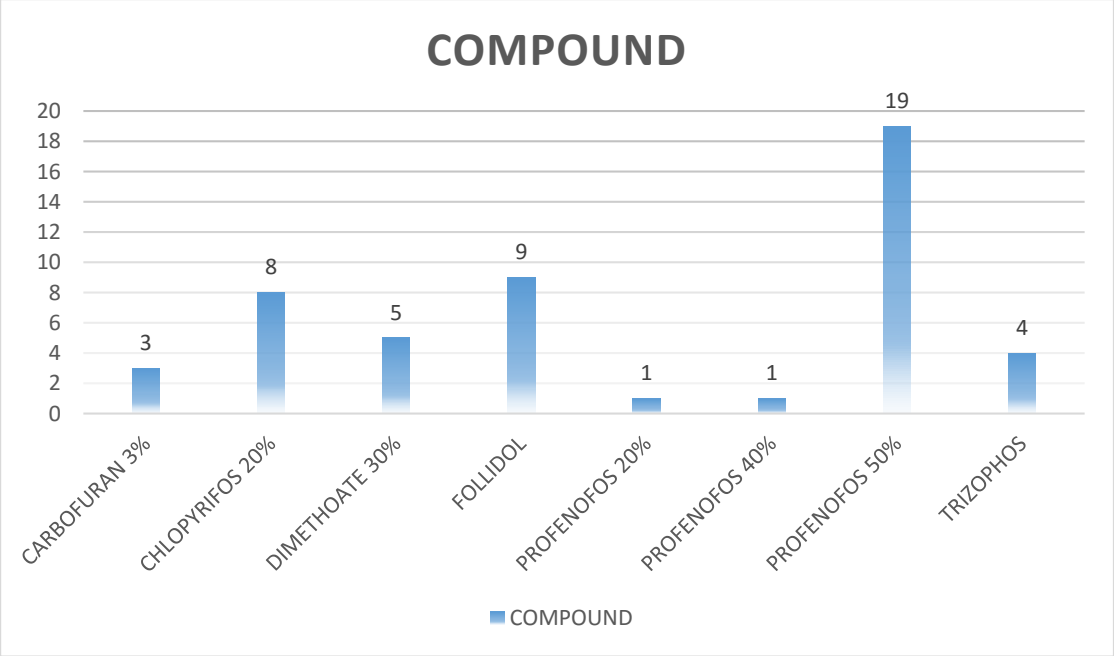


Table 6 Ingested with Alcohol or not?

ALCOHOL	No.of respondents (n=50)	Percentage (100%)
No	15	30.0
Yes	35	70.0

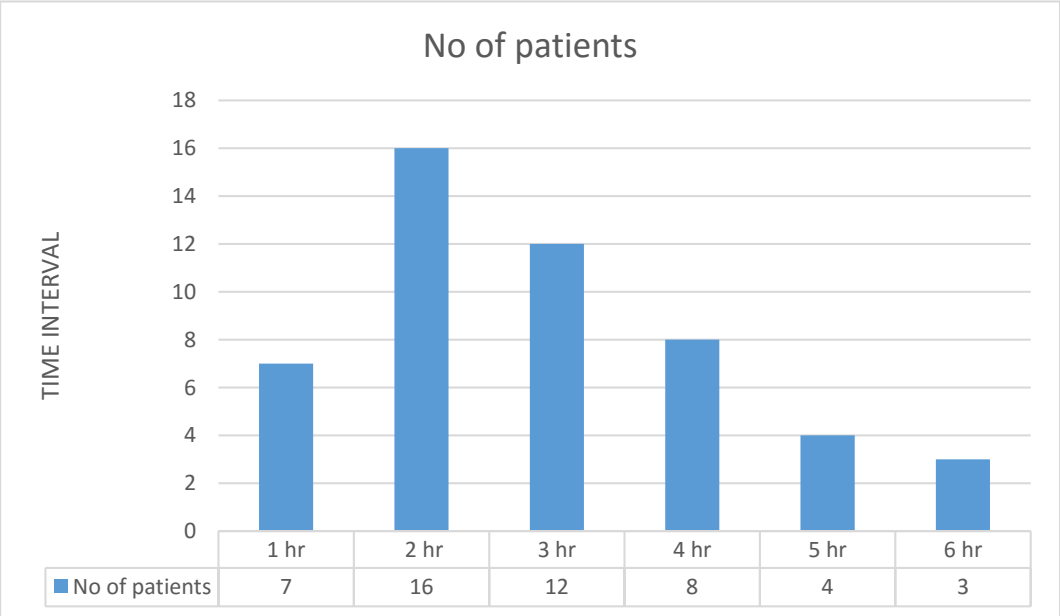
In this study, out of 50 patients, 35 patients (70%) consumed Organophosphate compound after mixing with alcohol.

DISTRIBUTION ACCORDING TO DURATION BETWEEN INGESTION OF ORGANOPHOSPHATES AND PRESENTATION TO ED

Table 7 Time interval between ingestion of poison and presentation to hospital

TIME INTERVAL (In hours)	No.of respondents (n=50)	Percentage (100%)
1	7	14.0
2	16	32.0
3	12	24.0
4	8	16.0
5	4	8.0
6	3	6.0

Most of the patients (32%) presented to the hospital within 2 hours of poisoning, 24% within 3 hours, 16% within 4 hours, and 14% within 1 hour.



SYMPTOMS	No.of respondents (n=50)	Percentage (100%)
No	1	2.0
Yes	49	98.0

TABLE 8 DISTRIBUTION ACCORDING TO PRESENCE OF SYMPTOMS

Except one patient all of the patients in the study group presented with symptoms of organophosphate poisoning with classical cholinergic features.

DISTRIBUTION ACCORDING TO SEVERITY BY BARDIN'S CLASSIFICATION

Table 9 BARDIN'S CLASSIFICATION

BARDIN	No.of respondents (n=50)	Percentage (100%)
1	11	22.0
2	20	40.0
3	19	38.0

Out if 50 patients in the study, 20 patients presented in grade II severity according to Bardin classification and 19 patients presented in Bardin grade III severity, And remaining 11 patients presented in Bardin severity grade I.

DISTRIBUTION ACCORDING TO VENTILATOR SUPPORT REQUIREMENT

TABLE 10 VENTILATOR SUPPORT REQUIREMENT

VENTILATOR	No.of respondents (n=50)	Percentage (100%)
No	21	42.0
Yes	29	58.0

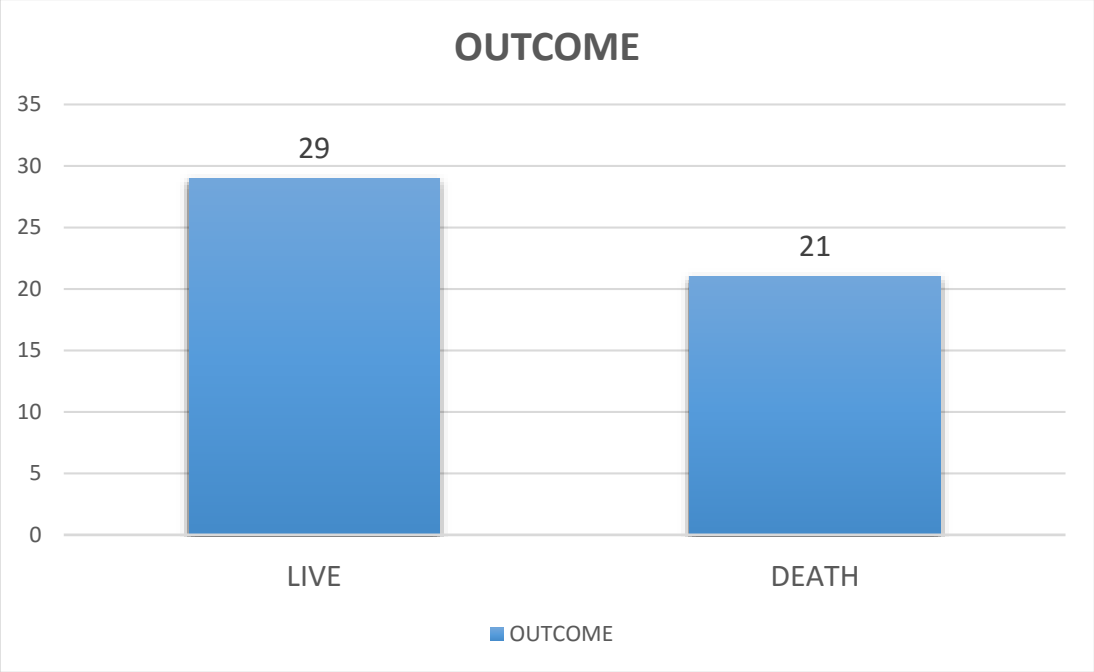
In this study out of 50 patients, 29 patients were ventilated for respiratory failure and 21 patients did not require ventilator support.

DISTRIBUTION ACCORDING TO THERAPEUTIC END POINT

Table 11 ACCORDING TO THERAPEUTIC END POINT

OUTCOME	No.of respondents (n=50)	Percentage (100%)
Death	21	42.0
Live	29	58.0

In this study, 29 patients had a successful therapeutic end point, and 21 patients expired inspite of appropriate treatment.

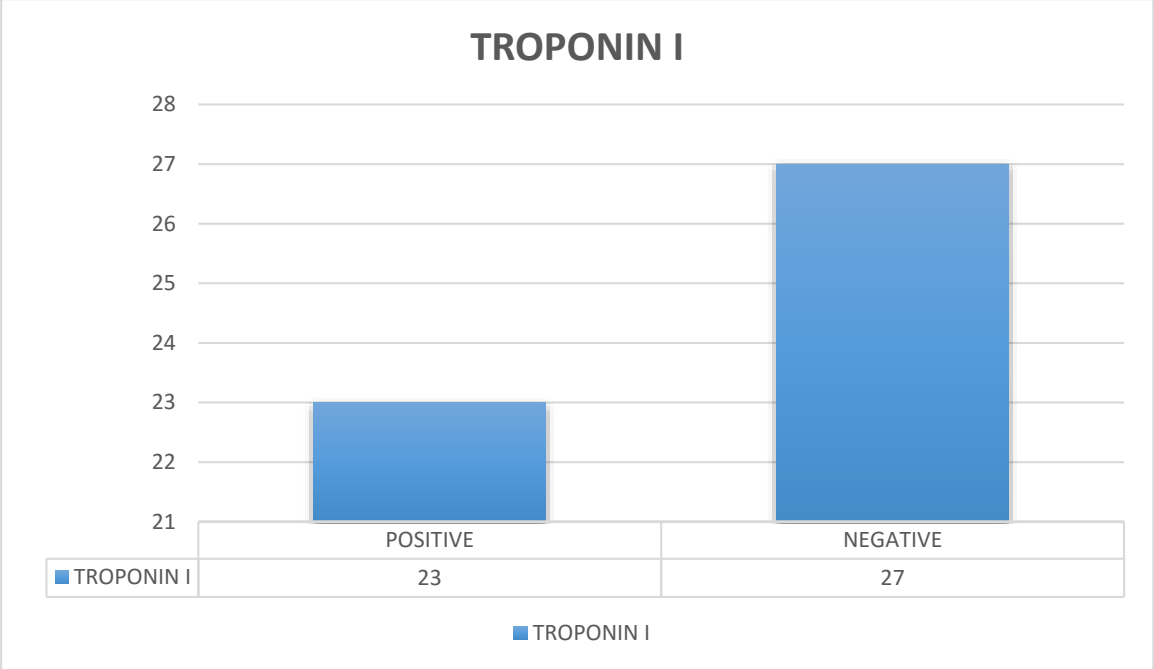


DISTRIBUTION ACCORDING TO TROPONIN I RESULT

Table 12 TROPONIN I RESULT

TROP I	No.of respondents (n=50)	Percentage (100%)
Negative	27	54.0
Positive	23	46.0

In this study of 50 patients, 23 patients had troponin I positivity and 27 patients had troponin I negative.



DESCRIPTIVE STATISTICS

Table 13 DESCRIPTIVE STATISTICS AGE, QUANTIITY, and TIME INTERVAL

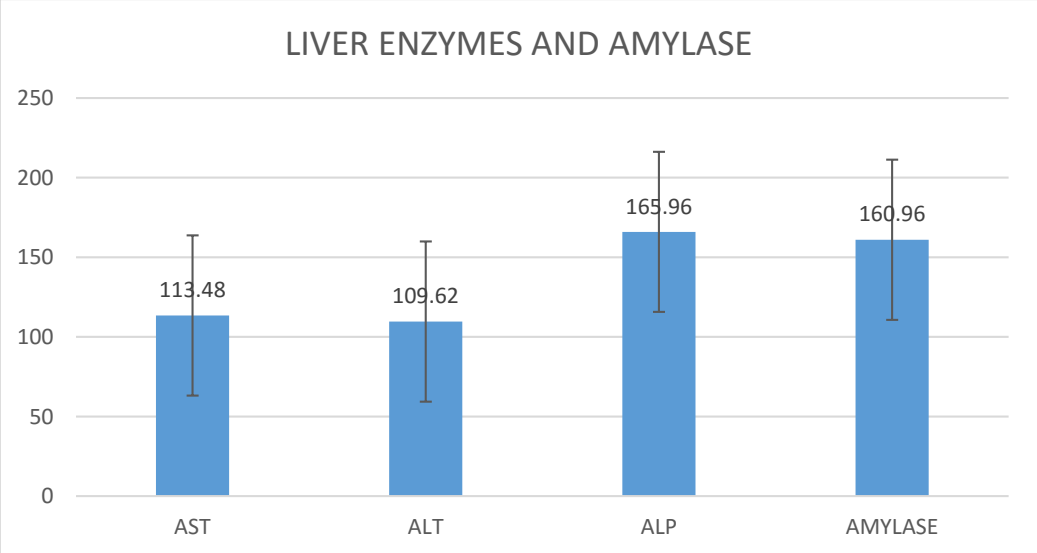
	N	Min.	Max	Mean	S.D
AGE (IN YEARS)	50	20	60	32.20	11.416
QUANTITY (IN ML)	50	50	250	145.20	61.053
TIME INT (IN HOURS)	50	1	6	2.90	1.389

In this study group, the mean age of presentation is 32.2 years with a standard deviation of 11.416. The mean quantity of poison ingested is 145.20 ml with a standard deviation of 61.053. The mean time interval of presentation is 2.90 hours with a standard deviation of 1.389.

ANALYSIS OF LIVER ENZYMES AND AMYLASE

Table 14 DESCRIPTIVE STATISTICS LIVER ENZYMES, AMYLASE

	N	Min.	Max	Mean	S.D
AST	50	20	220	113.48	50.287
ALT	50	18	220	109.62	50.004
ALP	50	48	362	165.96	82.646
AMYLASE	50	34	360	160.96	93.453



The mean values of AST-113.48 IU/L, ALT-109.62 IU/L, ALP- 165.96 IU/L, and Amylase- 160.96 IU/L is noted among the poisoning patients in this study.

ANALYSIS OF SERUM ELECTROLYTES

Table 15 DESCRIPTIVE STATISTICS SERUM ELECTROLYTES

	Min.	**Max**	**Mean**	**S.D**
SODIUM (IN MEQ/L)	126	144	134.90	3.370
POTASSIUM (IN MEQ/L)	2.60	3.80	3.2140	.22769

ANALYSIS OF CREATINE PHOSPHOKINASE

Table 16 DESCRIPTIVE STATISTICS CPK, CPK MB

	Min.	**Max**	**Mean**	**S.D**
CPK (IU/L)	30	3738	802.38	955.396
CPK-MB (IU/L)	15	758	191.76	207.497

CHI-SQUARE TEST TO COMPARE THE OUTCOMES WITH DIFFERENT AGE GROUPS

Table 17 THE OUTCOMES WITH DIFFERENT AGE GROUPS

AGE	**Death**		**Live**		**Total**		**Statistical inference**
	(n=21)	**(100%)**	**(n=29)**	**(100%)**	**(n=50)**	**(100%)**	
20 to 30yrs	15	71.4%	16	55.2%	31	62.0%	X^2=1.981 Df=3 .576>0.05 **Not Significant**
31 to 40yrs	2	9.5%	7	24.1%	9	18.0%	
41 to 50yrs	2	9.5%	3	10.3%	5	10.0%	
51 to 60yrs	2	9.5%	3	10.3%	5	10.0%	

There is no statistical significance when outcome is compared with different age groups of patients in this study group.

CHI-SQUARE TEST TO COMPARE THE OUTCOMES WITH SEX OF PATIENTS

Table 18 OUTCOMES WITH SEX OF PATIENTS

SEX	Death		Live		Total		Statistical inference
	(n=21)	(100%)	(n=29)	(100%)	(n=50)	(100%)	
Male	14	66.7%	23	79.3%	37	74.0%	X^2=1.012 Df=1 .314>0.05 **Not Significant**
Female	7	33.3%	6	20.7%	13	26.0%	

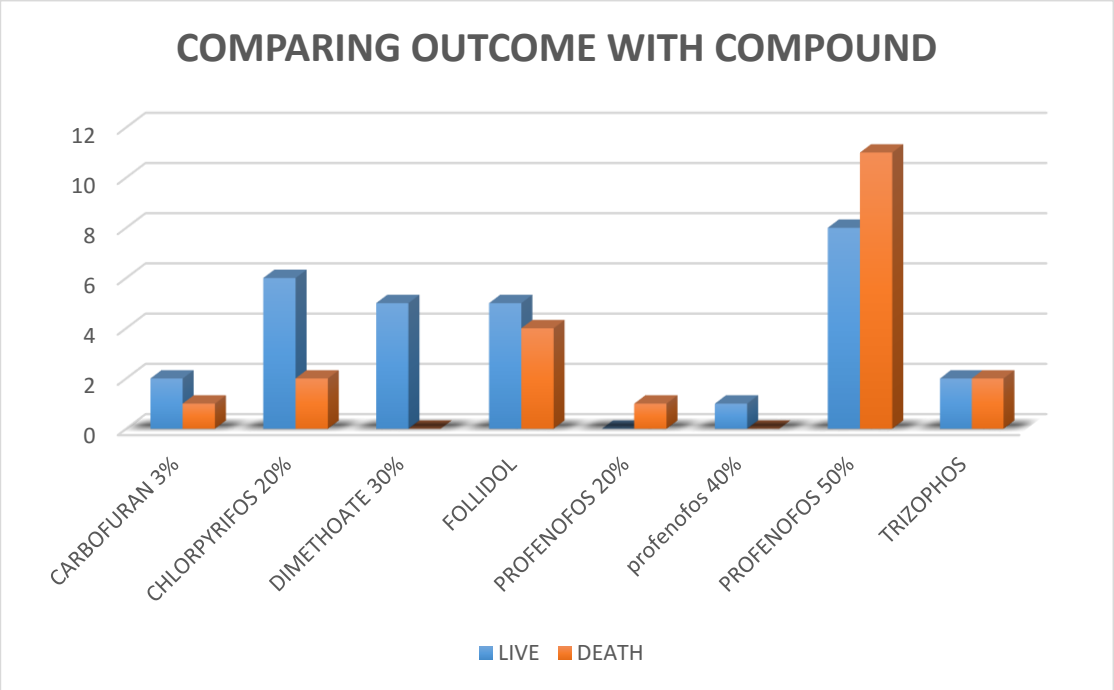
There is no statistical significance when outcome is compared with sex of the individuals in the study.

TO COMPARE THE OUTCOMES WITH COMPOUNDS BY CHI-SQUARE TEST

TABLE 19 OUTCOMES WITH COMPOUNDS

COMPOUND	Death		Live		Total		Statistical inference
	(n=21)	(100%)	(n=29)	(100%)	(n=50)	(100%)	
CARBOFURAN 3%	1	4.8%	2	6.9%	3	6.0%	X^2=8.865 Df=7 .262>0.05 **Not Significant**
CHLORPYRIFOS 20%	2	9.5%	6	20.7%	8	16.0%	
DIMETHOATE 30%	0	.0%	5	17.2%	5	10.0%	
FOLLIDOL	4	19.0%	5	17.2%	9	18.0%	

PROFENOFOS 20%	1	4.8%	0	.0%	1	2.0%	
PROFENOFOS 40%	0	.0%	1	3.4%	1	2.0%	
PROFENOFOS 50%	11	52.4%	8	27.6%	19	38.0%	
TRIZOPHOS	2	9.5%	2	6.9%	4	8.0%	



Using Chi-square test the overall outcome is compared with separate compounds involved in poisoning. Though maximal negative outcome is associated with profenofos 50%, the result is not statistically significant.

Table 20 ALCOHOL ALONG WITH OP COMPOUND

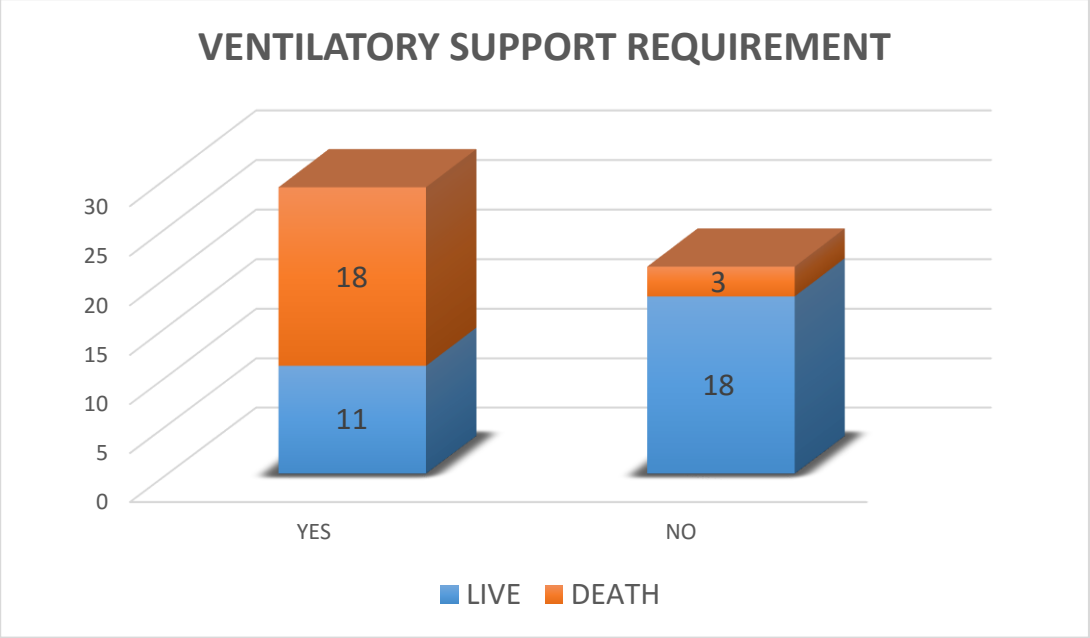
ALCOHOL	Death		Live		Total		Statistical inference
	(n=21)	(100%)	(n=29)	(100%)	(n=50)	(100%)	
No	5	23.8%	10	34.5%	15	30.0%	X^2=.661 Df=1 .416>0.05 **Not Significant**
Yes	16	76.2%	19	65.5%	35	70.0%	

On comparing the outcome of the patient with mixing of alcohol with the poison before ingestion, there is no statistically significance noted.

CHI-SQUARE TEST TO COMPARE THE OUTCOME WITH VENTILATORY SUPPORT REQUIREMENT

Table 21 OUTCOME WITH VENTILATORY SUPPORT REQUIREMENT

VENTILATOR	**Death**		**Live**		**Total**		**Statistical inference**
	(n=21)	**(100%)**	**(n=29)**	**(100%)**	**(n=50)**	**(100%)**	
No	3	14.3%	18	62.1%	21	42.0%	X^2=11.416 Df=1 .001<0.05 **Significant**
Yes	18	85.7%	11	37.9%	29	58.0%	



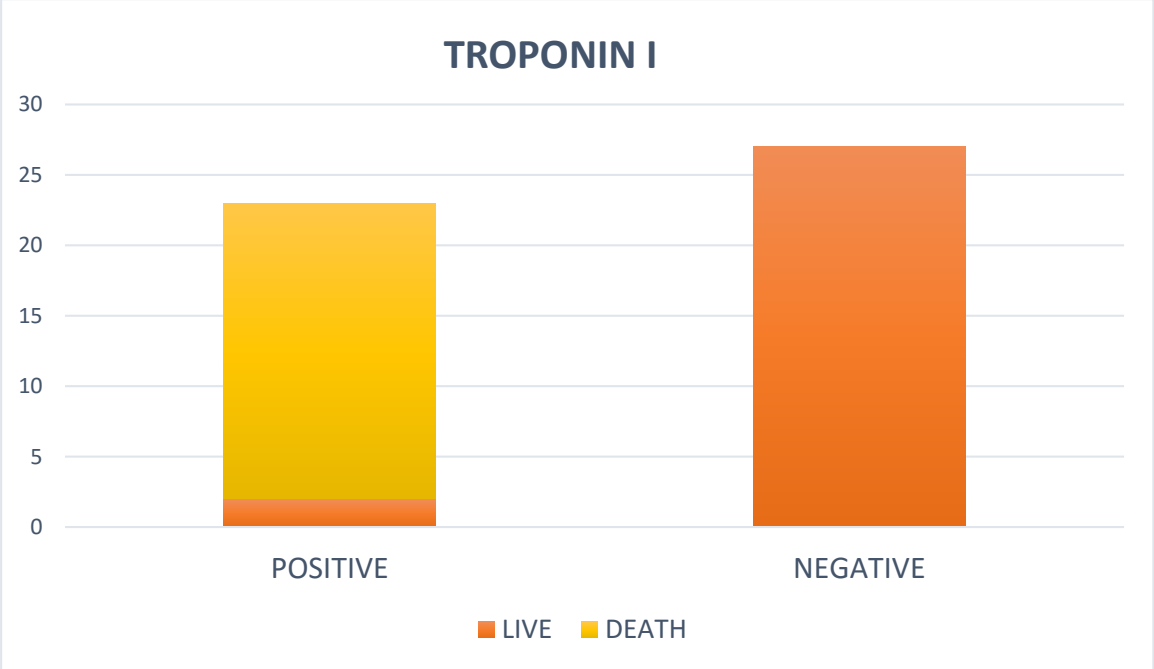
Comparing the outcome with the requirement for Ventilatory support following organophosphate poisoning has high statistical significance.

CHI-SQUARE TEST TO COMPARE THE OUTCOME WITH TROPONIN I

Table 22 COMPARE THE OUTCOME WITH TROPONIN I

TROP I	**Death**		**Live**		**Total**		**Statistical inference**
	(n=21)	**(100%)**	**(n=29)**	**(100%)**	**(n=50)**	**(100%)**	
Negative	0	.0%	27	93.1%	27	54.0%	X^2=42.504 Df=1 .000<0.05 **Significant**
Positive	21	100.0%	2	6.9%	23	46.0%	

In the study group, there is high statistical significance on comparing outcome of the patient with Troponin I. Most of the patients who had Troponin I positive had a negative outcome.



T – TEST TO ASSESS STATISTICAL SIGNIFICANCE OF VARIAOUS PARAMETERS

AGE	**Mean**	**S.D**	**Statistical inference**
Live (n=29)	32.90	11.040	T=.503 Df=48 .617>0.05 **Not significant**
Death (n=21)	31.24	12.124	

Table 23 AGE WITH OUTCOME

The mean age of patients who had successful outcome is 32.90 and mean age of patients with negative outcome is 31.24. There is no statistical significance using age as a predictor of outcome

Table 24 QUANTITY WITH OUTCOME

QUANTITY	Mean	S.D	Statistical inference
Live (n=29)	143.79	61.086	T=.190 Df=48 .850>0.05 **Not significant**
Death (n=21)	147.14	62.461	

The mean quantity of poison ingested among the patients who survived is 143.79 ml and the mean quantity of poison ingested among patients who expired is 147.14 ml. There is no statistical significance noted using quantity of poison ingested as a predictor of outcome.

Table 25 TIME INTERVAL WITH OUTCOME

TIME INT	Mean	S.D	Statistical inference
Live (n=29)	2.45	1.152	T=-2.900 Df=48 .006<0.05 **Significant**
Death (n=21)	3.52	1.470	

The average time interval between ingestion of organophosphate and presentation to emergency department for a successful outcome is 2.45 hours and a negative outcome is 3.52 hours. It is statistically significant and hence duration between ingestion of poison and admission to hospital can be used as a predictor of outcome.

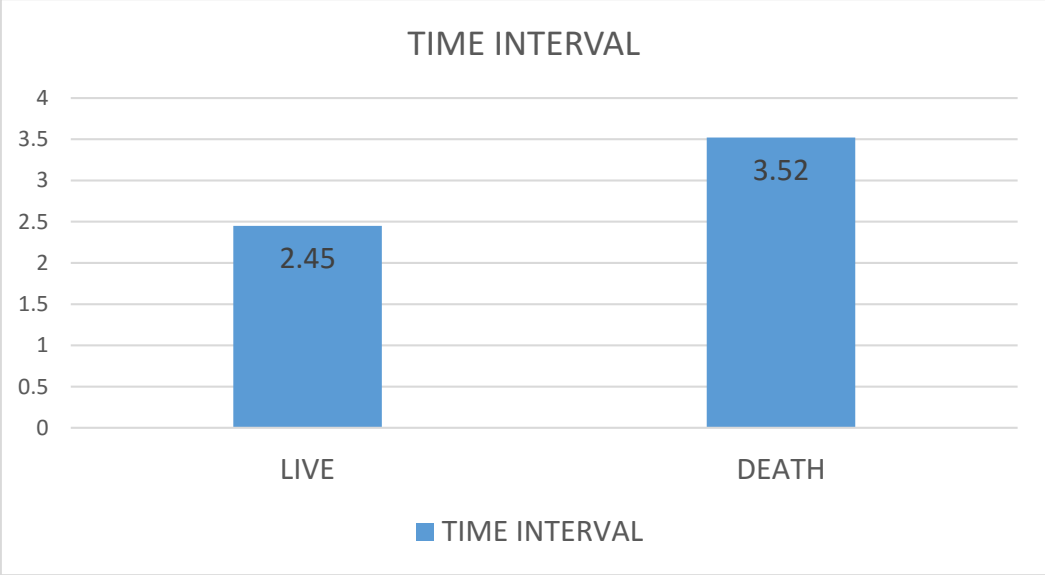


Table 26 ENZYMES WITH OUTCOME

AST	**Mean**	**S.D**	**Statistical inference**
Live (n=29)	102.24	50.026	T=-1.906 Df=48 .063>0.05 Not significant
Death (n=21)	129.00	47.494	
ALT	**Mean**	**S.D**	**Statistical inference**
Live (n=29)	93.31	50.985	T=-2.909 Df=48 .005<0.05 **Significant**
Death (n=21)	132.14	39.603	
ALP	**Mean**	**S.D**	**Statistical inference**
Live (n=29)	157.90	76.705	T=-.808 Df=48 .423>0.05 Not significant
Death (n=21)	177.10	90.954	
AMYLASE	**Mean**	**S.D**	**Statistical inference**
Live (n=29)	140.59	84.798	T=-1.856 Df=48 .070>0.05 Not significant
Death (n=21)	189.10	99.484	

The mean AST in patients who survived is 102.24 and 129.00 in patients who expired. Since p value is >0.05 it is not statistically significant to predict outcome.

The mean ALT in patients who survived is 93.31 and it is 132.14 in patients who expired. Since p value is <0.05 it is statistically significant to predict outcome.

The mean Amylase in patients who survived is 140.59 and it is 189.10 in patients who expires. Since p value is >0.05 it is not statistically significant to predict outcome.

Table 27 ELECTROLYTES WITH OUTCOME

SODIUM	**Mean**	**S.D**	**Statistical inference**
Live (n=29)	135.41	3.123	T=1.275 Df=48 .208>0.05 Not significant
Death (n=21)	134.19	3.642	
POTASSIUM	**Mean**	**S.D**	**Statistical inference**
Live (n=29)	3.2690	.23468	T=2.072 Df=48 .044<0.05 **Significant**
Death (n=21)	3.1381	.19869	

The mean Serum Sodium in patients who survived is 135.41 and in patients who expired is 134.19. The p value is >0.05 and hence it is not statistically significant and thus cannot be used to predict outcome.

The mean serum potassium is 3.269 in patients who survived and it is 3.1381 in patients who expired. Since the P value is <0.05 it is statistically significant and hence can be used as a predictor of outcome.

Table 28 SchE with outcome

S.AchE	Mean	S.D	Statistical inference
Live (n=29)	2357.34	2242.477	T=3.096 Df=48 .003<0.05 **Significant**
Death (n=21)	821.00	399.836	

The mean serum cholinesterase in patients who survived is 2357.34 and in those patients who expired it is 821.00 and it gives a P value of <0.05. It is statistically significant to be used as a predictor of outcome.

Table 29 CPK & CPK MB with outcome

CPK	Mean	S.D	Statistical inference
Live (n=29)	444.76	621.248	T=-3.436 Df=48 .001<0.05 **Significant**
Death (n=21)	1296.24	1120.022	
CPK-MB	**Mean**	**S.D**	**Statistical inference**
Live (n=29)	81.72	93.538	T=-5.613 Df=48 .000<0.05 **Significant**
Death (n=21)	343.71	226.792	

The mean CPK for the patients who survived is 444.76 and for the patients who expired it is 1296.24. The p value is <0.05 and it is statistically significant and thus can be used as a predictor of outcome.

The mean CPK MB for the patients who survived is 81.72 and for the patients who expired it is 343.71. The p value is <0.05 and it is statistically significant and thus can be used as a predictor of outcome.

The study group 50 patients are classified into 4 groups depending on the serum cholinesterase levels.

S. AchE activity	**No.of respondents (n=50)**	**Percentage (100%)**
< 10%	9	18.0
10 - 20%	15	30.0
20 – 50%	15	30.0
> 50%	11	22.0

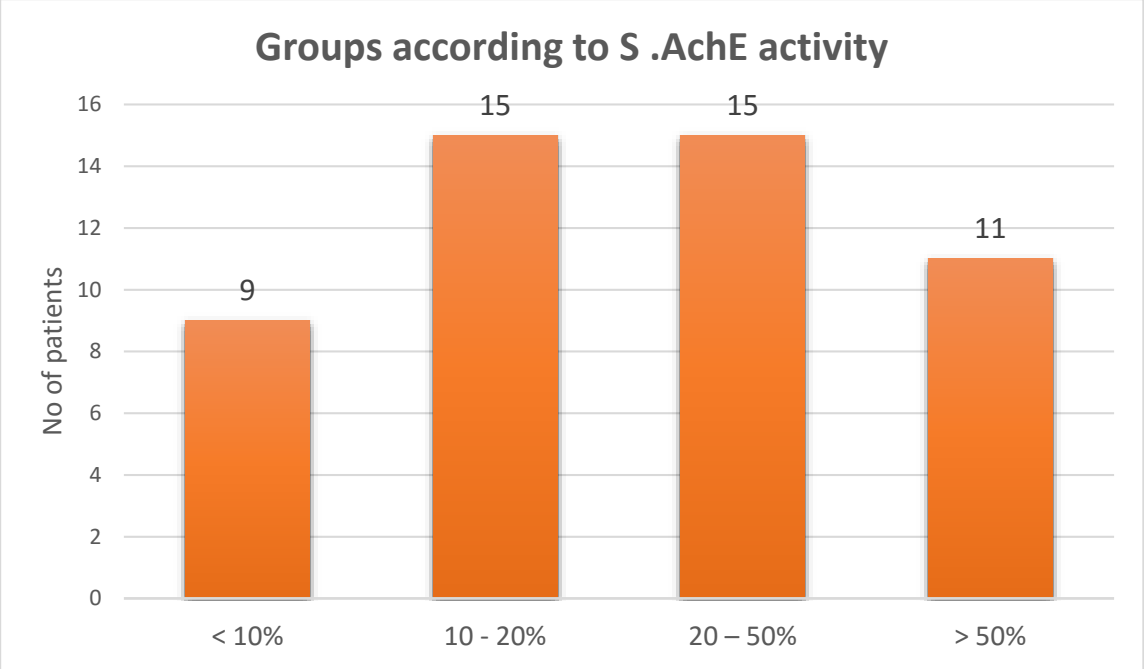
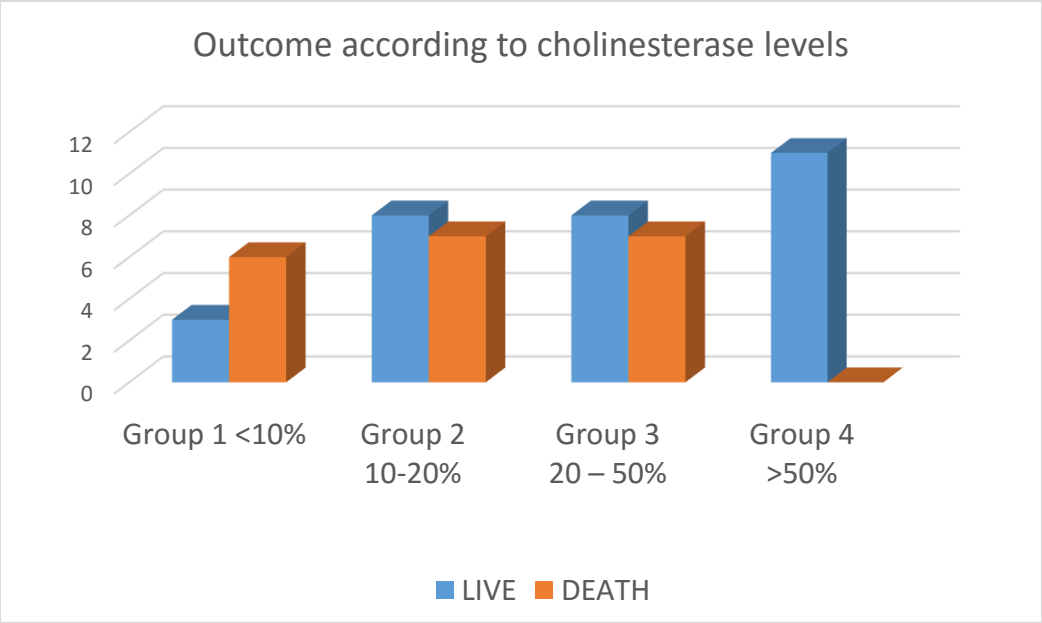


TABLE 30 SCHE ACTIVITY AND OUTCOME

S. AchE activity	OUTCOME						Statistical inference
	Death		Live		Total		
	(n=21)	(100%)	(n=29)	(100%)	(n=50)	(100%)	
Group 1 <10%	6	28.6%	3	10.3%	9	18.0%	X^2=11.138 Df=3 .011<0.05 **Significant**
Group 2 10-20%	7	33.3%	8	27.6%	15	30.0%	
Group 3 20 – 50%	8	38.1%	7	24.1%	15	30.0%	
Group 4 >50%	0	.0%	11	37.9%	11	22.0%	

According to the serum cholinesterase levels, the study patients are categorised into 4 groups, Group 1 having the lowest enzyme activity of < 10% and group 5 having an enzyme activity of > 50 %. Most of the patients having enzyme activity < 10 % had a negative outcome and those who had > 50%

enzyme activity had a successful outcome and it is statistically significant. Thus Cholinesterase enzyme activity can be used as a predictor of outcome.



ANALYSIS OF VARIATIONS IN PARAMETERS COMPARING WITH THE COMPOUNDS USING ONEWAY ANOVA

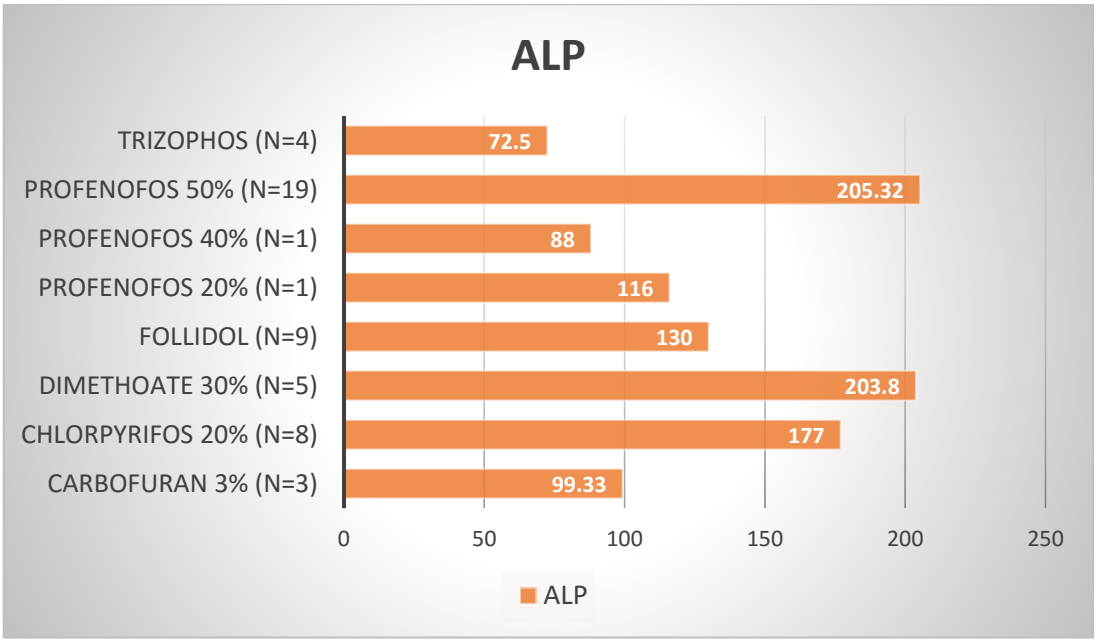
Table 31 VARIATIONS IN PARAMETERS COMPARING WITH THE COMPOUNDS

AST	Mean	S.D	Statistical inference
CARBOFURAN 3% (n=3)	87.33	86.731	F=.968 .467>0.05 Not significant
CHLORPYRIFOS 20% (n=8)	127.25	20.865	
DIMETHOATE 30% (n=5)	108.60	61.329	
FOLLIDOL (n=9)	125.11	39.397	
PROFENOFOS 20% (n=1)	107.00	.	
profenofos 40% (n=1)	120.00	.	
PROFENOFOS 50% (n=19)	118.95	55.070	
TRIZOPHOS (n=4)	59.50	46.737	
ALT	**Mean**	**S.D**	**Statistical inference**
CARBOFURAN 3% (n=3)	76.00	49.960	F=1.087 .389>0.05
CHLORPYRIFOS 20% (n=8)	124.50	27.034	

DIMETHOATE 30% (n=5)	88.40	42.341	Not significant
FOLLIDOL (n=9)	113.89	35.364	
PROFENOFOS 20% (n=1)	82.00	.	
profenofos 40% (n=1)	18.00	.	
PROFENOFOS 50% (n=19)	119.68	54.350	
TRIZOPHOS (n=4)	104.00	88.095	
ALP	**Mean**	**S.D**	**Statistical inference**
CARBOFURAN 3% (n=3)	99.33	8.327	F=2.782 .018<0.05 **significant**
CHLORPYRIFOS 20% (n=8)	177.00	46.043	
DIMETHOATE 30% (n=5)	203.80	90.511	
FOLLIDOL (n=9)	130.00	69.937	
PROFENOFOS 20% (n=1)	116.00	.	
profenofos 40% (n=1)	88.00	.	
PROFENOFOS 50% (n=19)	205.32	88.357	
TRIZOPHOS (n=4)	72.50	20.421	
AMYLASE	**Mean**	**S.D**	**Statistical inference**
CARBOFURAN 3% (n=3)	141.00	64.133	F=2.522 .029<0.05 **significant**
CHLORPYRIFOS 20% (n=8)	169.63	85.634	
DIMETHOATE 30% (n=5)	100.20	24.294	
FOLLIDOL (n=9)	120.11	46.812	
PROFENOFOS 20% (n=1)	223.00	.	
profenofos 40% (n=1)	44.00	.	
PROFENOFOS 50% (n=19)	213.84	109.769	
TRIZOPHOS (n=4)	89.00	40.669	
SODIUM	**Mean**	**S.D**	**Statistical inference**
CARBOFURAN 3% (n=3)	134.67	2.309	F=2.496 .031<0.05 **significant**
CHLORPYRIFOS 20% (n=8)	134.25	1.581	
DIMETHOATE 30% (n=5)	139.40	3.507	

FOLLIDOL (n=9)	133.67	1.581	
PROFENOFOS 20% (n=1)	132.00	.	
profenofos 40% (n=1)	132.00	.	
PROFENOFOS 50% (n=19)	135.42	3.254	
TRIZOPHOS (n=4)	132.50	5.916	
POTASSIUM	**Mean**	**S.D**	**Statistical inference**
CARBOFURAN 3% (n=3)	3.5000	.36056	F=1.310 .270>0.05 Not significant
CHLORPYRIFOS 20% (n=8)	3.1625	.17678	
DIMETHOATE 30% (n=5)	3.3000	.25495	
FOLLIDOL (n=9)	3.2333	.21794	
PROFENOFOS 20% (n=1)	3.1000	.	
profenofos 40% (n=1)	3.0000	.	
PROFENOFOS 50% (n=19)	3.1579	.22439	
TRIZOPHOS (n=4)	3.3000	.14142	
CALCIUM	**Mean**	**S.D**	**Statistical inference**
CARBOFURAN 3% (n=3)	8.3667	.37859	F=2.114 .063>0.05 Not significant
CHLORPYRIFOS 20% (n=8)	8.0125	.36031	
DIMETHOATE 30% (n=5)	8.1200	.43243	
FOLLIDOL (n=9)	6.8111	1.37609	
PROFENOFOS 20% (n=1)	7.2000	.	
profenofos 40% (n=1)	7.9000	.	
PROFENOFOS 50% (n=19)	7.9842	1.01886	
TRIZOPHOS (n=4)	8.3000	.14142	
CPK	**Mean**	**S.D**	**Statistical inference**
Between Groups			F=1.340 .256>0.05 Not significant
CARBOFURAN 3% (n=3)	1332.00	2083.677	
CHLORPYRIFOS 20% (n=8)	925.38	780.021	
DIMETHOATE 30% (n=5)	610.20	1141.352	

FOLLIDOL (n=9)	502.67	683.104	
PROFENOFOS 20% (n=1)	2738.00	.	
profenofos 40% (n=1)	30.00	.	
PROFENOFOS 50% (n=19)	929.74	901.981	
TRIZOPHOS (n=4)	178.00	99.022	
CPK-MB	**Mean**	**S.D**	**Statistical inference**
CARBOFURAN 3% (n=3)	195.00	306.588	F=2.219 0.52>0.05 Not significant
CHLORPYRIFOS 20% (n=8)	221.38	220.552	
DIMETHOATE 30% (n=5)	55.00	45.404	
FOLLIDOL (n=9)	147.11	162.806	
PROFENOFOS 20% (n=1)	758.00	.	
profenofos 40% (n=1)	23.00	.	
PROFENOFOS 50% (n=19)	240.21	207.062	
TRIZOPHOS (n=4)	72.00	80.784	
S.AchE	**Mean**	**S.D**	**Statistical inference**
CARBOFURAN 3% (n=3)	4653.00	4089.317	F=2.301 .044<0.05 **significant**
CHLORPYRIFOS 20% (n=8)	1339.88	1337.882	
DIMETHOATE 30% (n=5)	1339.00	720.220	
FOLLIDOL (n=9)	1807.00	1697.805	
PROFENOFOS 20% (n=1)	410.00	.	
profenofos 40% (n=1)	802.00	.	
PROFENOFOS 50% (n=19)	1200.95	827.634	
TRIZOPHOS (n=4)	3484.50	3715.957	


ALP
TRIZOPHOS (N=4)
PROFENOFOS 50% (N=19)
PROFENOFOS 40% (N=1)
PROFENOFOS 20% (N=1)
FOLLIDOL (N=9)
DIMETHOATE 30% (N=5)
CHLORPYRIFOS 20% (N=8)
CARBOFURAN 3% (N=3)
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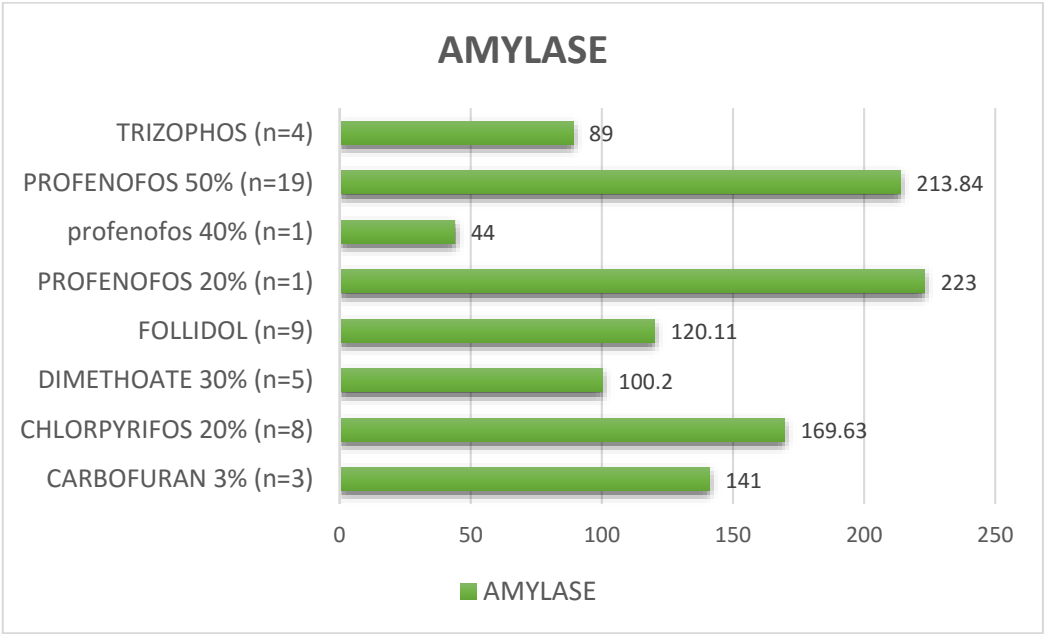
ALP


AMYLASE
TRIZOPHOS (n=4)
PROFENOFOS 50% (n=19)
profenofos 40% (n=1)
PROFENOFOS 20% (n=1)
FOLLIDOL (n=9)
DIMETHOATE 30% (n=5)
CHLORPYRIFOS 20% (n=8)
CARBOFURAN 3% (n=3)
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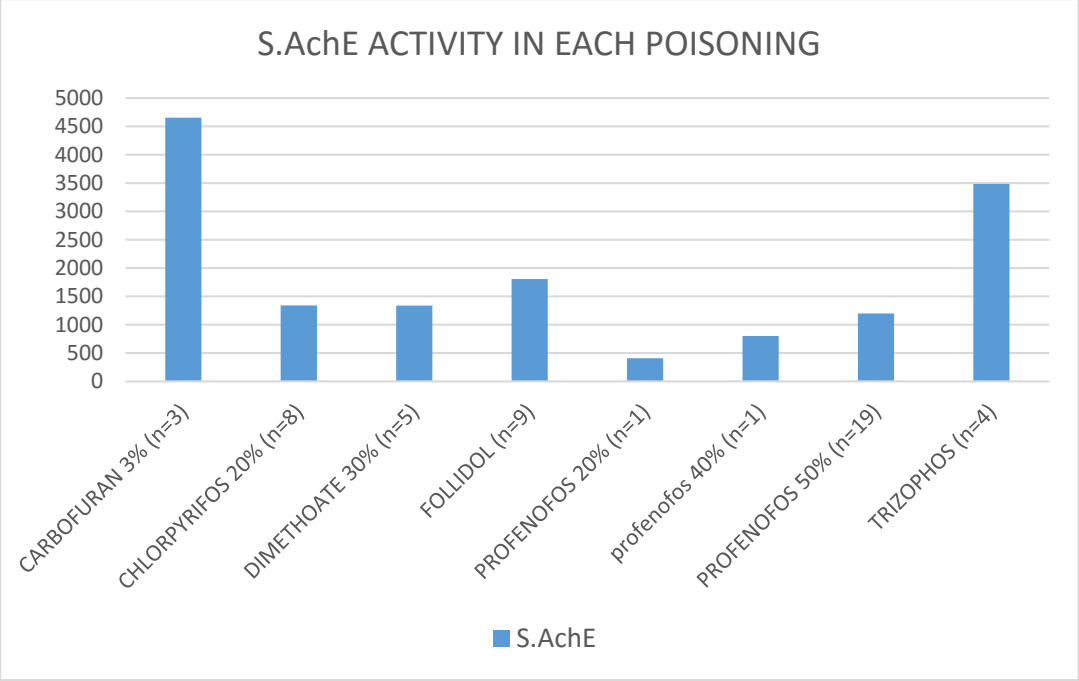
AMYLASE



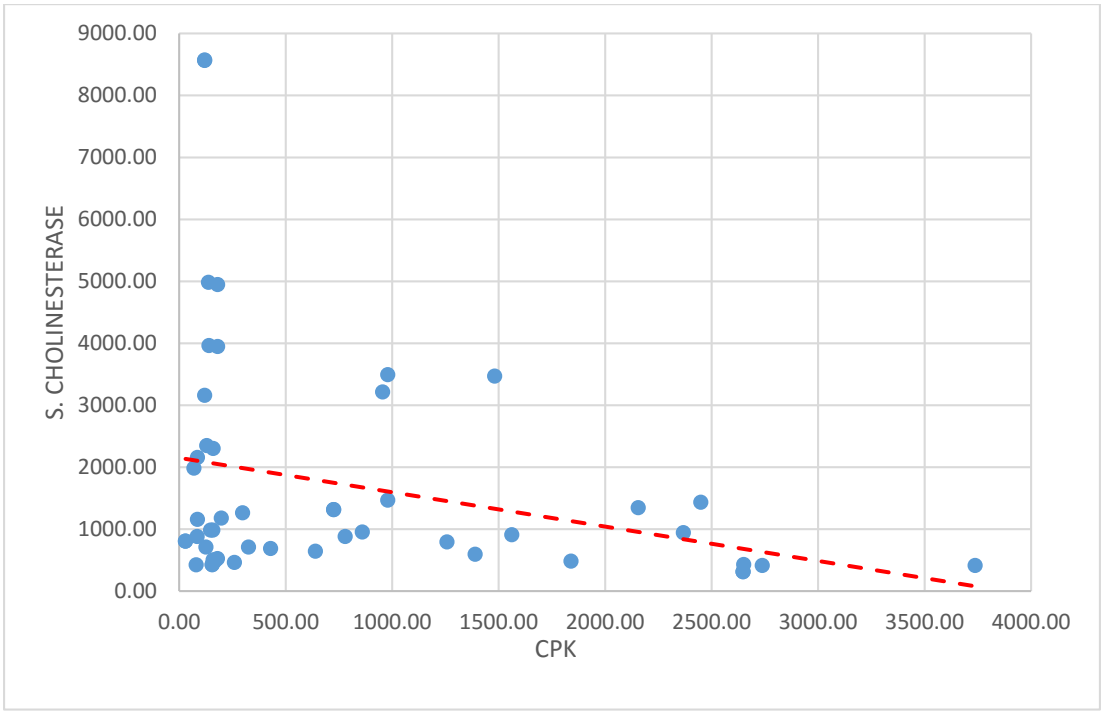
By using One-way ANOVA, variations in the individual parameters is compared with the compound ingested in poisoning. Though there are huge variations in individual parameters caused by the organophosphate compounds not all turned out to be statistically significant. Elevation in ALP, Amylase, change in Serum Sodium, and fall in serum cholinesterase levels are all statistically significant when compared with individual compounds.

INTERCORRELATION BETWEEN THE VARIABLES

Table 32 INTERCORRELATION BETWEEN THE VARIABLES

	Mean	**S.D**		AST	ALT	ALP	AMYLASE	SODIUM	POTASSIUM	CALCIUM	CPK	CPK-MB	S.AchE
AST	113.48	50.287	r	1	.683(**)	.426(**)	.340(*)	-.064	-.471(**)	-.135	.273	.256	-.359(*)
			Sig.	.	.000	.002	.016	.661	.001	.348	.055	.073	.010
ALT	109.62	50.004	r	.683(**)	1	.409(**)	.336(*)	-.181	-.376(**)	-.041	.243	.235	-.319(*)
			Sig.	.000	.	.003	.017	.208	.007	.777	.089	.100	.024
ALP	165.96	82.646	r	.426(**)	.409(**)	1	.519(**)	.293(*)	-.227	.340(*)	.296(*)	.136	-.269
			Sig.	.002	.003	.	.000	.039	.113	.016	.037	.346	.059
AMYLASE	160.96	93.453	r	.340(*)	.336(*)	.519(**)	1	-.083	-.308(*)	.192	.442(**)	.403(**)	-.222
			Sig.	.016	.017	.000	.	.567	.029	.181	.001	.004	.122
SODIUM	134.90	3.370	r	-.064	-.181	.293(*)	-.083	1	.183	.031	-.097	-.191	.111
			Sig.	.661	.208	.039	.567	.	.204	.830	.503	.183	.443
POTASSIUM	3.2140	.22769	r	-.471(**)	-.376(**)	-.227	-.308(*)	.183	1	.119	-.096	-.350(*)	.424(**)
			Sig.	.001	.007	.113	.029	.204	.	.409	.508	.013	.002
CALCIUM	7.8220	.99453	r	-.135	-.041	.340(*)	.192	.031	.119	1	.284(*)	.015	-.085
			Sig.	.348	.777	.016	.181	.830	.409	.	.046	.915	.557

CPK	802.38	955.396	r	.273	.243	.296(*)	.442(**)	-.097	-.096	.284(*)	1	.646(**)	-.281(*)
			Sig.	.055	.089	.037	.001	.503	.508	.046	.	.000	.048
CPK-MB	191.76	207.497	r	.256	.235	.136	.403(**)	-.191	-.350(*)	.015	.646(**)	1	-.305(*)
			Sig.	.073	.100	.346	.004	.183	.013	.915	.000	.	.032
S.AchE	1712.08	1877.635	r	-.359(*)	-.319(*)	-.269	-.222	.111	.424(**)	-.085	-.281(*)	-.305(*)	1
			Sig.	.010	.024	.059	.122	.443	.002	.557	.048	.032	.
			n	50	50	50	50	50	50	50	50	50	50
*** Correlation is significant at the 0.01 level* * Correlation is significant at the 0.05 level*													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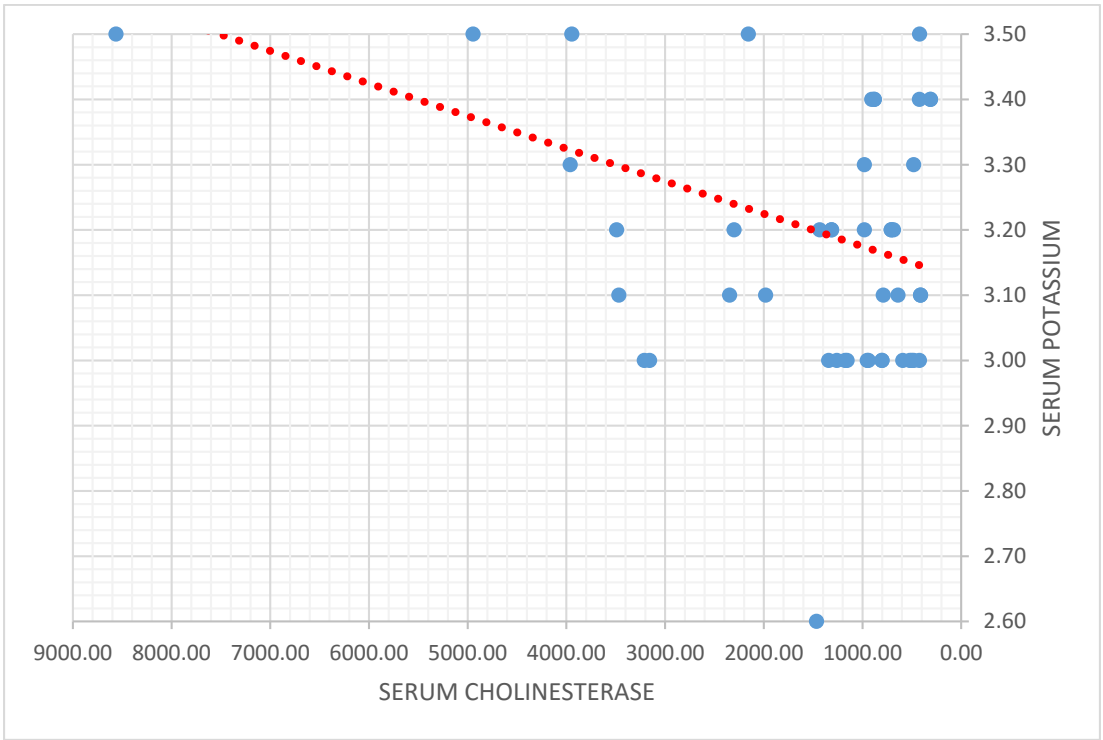
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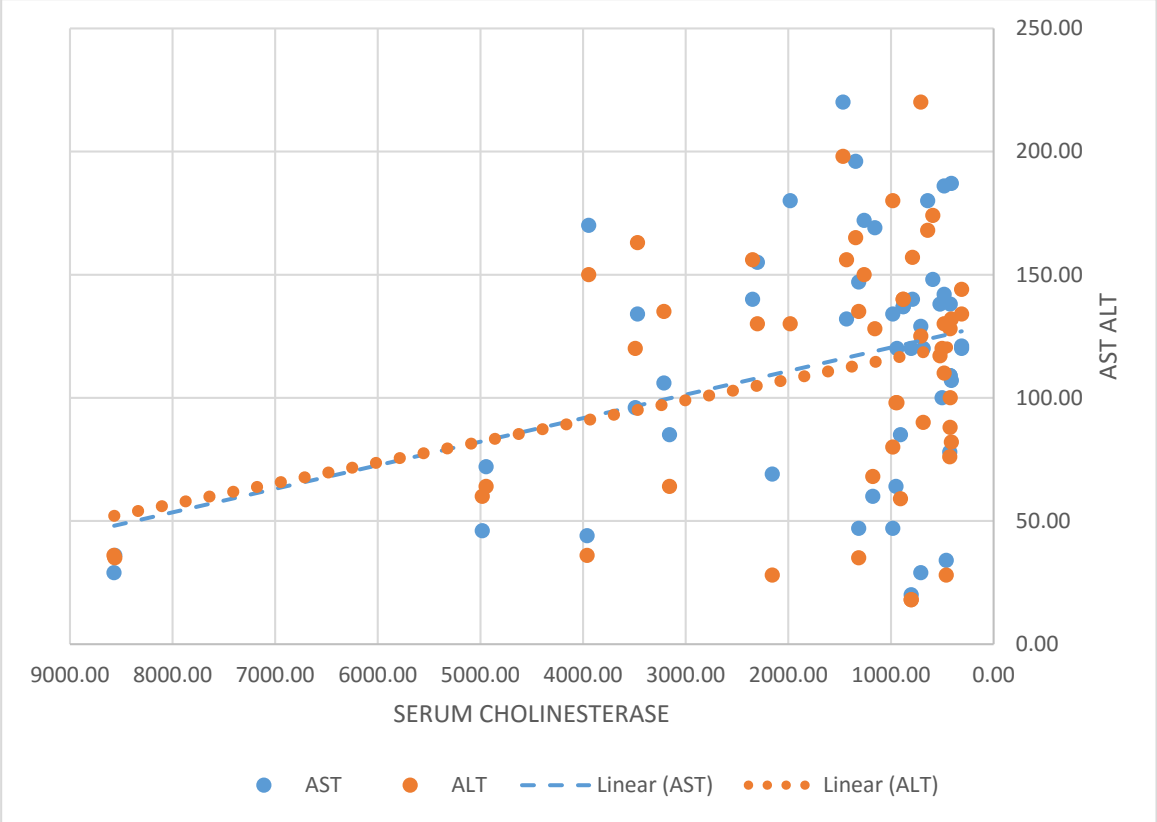
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Linear (ALT)

DISCUSSION

Organophosphate compounds are widely used as insecticide in agriculture. For the reason that they are easily available, accessible and used widely, organophosphate toxicity is a significant universal health concern mainly in unindustrialized countries. Hundreds of thousands of deaths happen worldwide because of organophosphate agents. Organophosphate ingestion is one of the supreme cause of suicidal deaths in India. The incidence of pesticide poisoning is very common among people of low socio economic status. It may be because of rapid urbanisation, economic and social factors that contribute to depression and frustration in people. Those persons are the major victims of poisoning, when they are not able to cope up with this stressful situations.

Inhibition of acetylcholinesterase is the main mechanism by which organophosphates act leading to excessive cholinergic stimulation. The clinical features of cholinergic storm develops fast, which helps in diagnosing clinically that is established by detailed history and biochemical demonstration of cholinesterase inhibition. This study is undertaken to analyse the biochemical abnormalities in organophosphate poisoning and to assess their prognostic significance.

In this study the total number of patients were 50. Among them 37 of them were male (74%) and 13 of them were female (26%), showing that the incidence of poisoning is more in males (Table 1). Among the study group, most of the individuals (62%) fall in the age-group of 20 to 30 years (Table 2).

This being the most critical period, when the person is likely to face many problems leading to psychological stress thus taking drastic steps to end the life by consuming toxic substances. There is no statistical significance when Age of the patient is compared with the outcome (Table 15) and hence it cannot be used as a prognostic indicator.

Among the OP agents the most common compound involved in this study is Profenofos 50% (n=19) and the next being Follidol (n=9) (Table 3). There is no statistical significance when individual compounds are compared with the patients' outcome (Table 17) and hence the OP agent involved in poisoning does not predict the outcome.

Mixing of alcohol with the OP compound before ingestion is seen in 35 patients (Table 4). Concurrent alcohol and organophosphate consumption is common in alcoholic patients, which can lead to consumption of higher amounts of OP compounds leading to higher levels of the OP agents in blood and higher chance of deaths. This is documented by Eddleston et al[(94)], but the fact taking alcohol along with OP compounds did not affect the outcome in this study (Table 18).

Most of the patients in this study presented to hospital within 2 - 3 hours (66%) (Table - 5). The average time interval from ingestion of OP agent and admission to our emergency ward for a successful outcome is 2.45 hours (Table 23), when it exceeds 3.52 hours the outcome is negative. It is statistically significant with a P value of <0.05 and hence can be used as a prognostic indicator.

In the study patients, the mean quantity of poison ingested is 145.20 ml with a SD 61.05. In patients who survived the mean quantity of poison ingested is 143.79 ml and those who had a negative outcome ingested 147.14 ml. The test of significance gives a P value of 0.850 and hence this parameter does not predict the outcome.

Out of 50 patients, 29 patients required ventilator support during the course of illness in the hospital (Table-8). Out of 29 patients who required ventilator support, 18 patients expired. Statistically this is significant with a P value of 0.001 <0.05. Hence ventilator requirement can be used to predict outcome.

The mean values of AST-113.48 IU/L, ALT-109.62 IU/L, ALP- 165.96 IU/L, and Amylase- 160.96 IU/L is noted among the poisoning patients in this study. According to Lohitnavy & Vijayaraghavan[95, 96], there is elevation of Serum AST and ALT because of degeneration of hepatocytes and further necrosis, causing damage to cell organelles like mitochondria and pouring these enzymes into blood stream[97, 98]. The present study also demonstrates elevation in liver enzymes following OP poisoning (Table 24). Among the liver enzymes ALT elevation shows a statistical significance when compared with the outcome and thus can be used as a prognostic indicator. Singh et al[99] found elevation of amylase and acute pancreatitis in OP poisoning. Matsumiya N et al[100] and Li T Nagayama N et al[101] stated that elevated serum amylase in the absence of clinical pancreatitis could be attributed to hypoxemia. Dressel et al[102] showed that OP intoxication causes increase in intraductal pressure and

increase in exocrine pancreas flow rate resulting in extravasation of fluid. Lin CL et al[103] showed that mean amylase level is elevated in patients requiring mechanical ventilation and a poorer outcome and a significant negative correlation with serum cholinesterase. In our study though there is a negative correlation between serum amylase and serum cholinesterase (Table 30) it is not found statistically significant. When comparing serum amylase with outcome, according to Sumathi et al[104] serum amylase is a good predictor of outcome, but in our study there is no statistical significance.

The mean serum potassium in our study is 3.2 meq/l (Table 13). According to Devanur RMM and Prasad et al[105], poor outcome in OP poisoning was noted in patients having respiratory distress with hypokalaemia and very low serum cholinesterase. They also found that there was a remarkable fall in serum potassium relating to OP toxicity induced weakness of muscle and paralysis finally leading to death. The fall in serum potassium was proportional to the onset of detrimental signs and symptoms. In our study the mean potassium in patients with successful outcome is 3.2 and in patients who had a negative endpoint is 3.13. The p value for statistical significance is <0.05 and hence Serum potassium can be used as a predictor of outcome.

The mean CPK in our study is 802.38 IU/L and CPK MB is 191.76 IU/L (Table 14. In a study conducted in Egypt by Nermeen AM et al [106] they have demonstrated increases in serum CPK and a proportionate fall in serum cholinesterase. The excess of acetylcholine in OP poisoning causes reversible muscle injury and rise in various muscle enzymes including CPK[107].

Dayanand Raddi et al conducted a study regarding CPK and OP poisoning and concluded escalation of CPK is evident of respiratory-failure and timely estimation of CPK has to be customarily taken as a prognostic indicator in OP poisoning[108].). In acute OP poisoning many cardiac events like arrhythmias, non-cardiogenic pulmonary edema, hypertension, conduction defects, and ECG changes like transient ST elevation have been documented[109]. The mechanism behind cardio toxicity of Organophosphates is not known. It is postulated that parasympathetic and sympathetic over activity causes myocardial damage. Parasympathetic over activity has significant role in coronary artery spasm[109, 110]. In a study conducted by Abbas Aghabiklooei et al [111], they have found out elevation of cardiac enzymes in acute OP poisoning and concluded myocardial involvement as a most significant cause of negative outcome in OP poisoning. They also hypothesised myocardial involvement as a good predictor of negative outcome in OP poisoning. In our study also there is a significant correlation between CPK, CPK MB (Table 27), and Troponin I (Table 10, 20) and the outcome of patient. Hence these three parameters can be used as a prognostic indicator in OP poisoning.

In our study serum cholinesterase mean value in patients who had successful outcome is 2357 IU/L and it is 821 IU/L in those who had a negative outcome. According to the cholinesterase values, patients are grouped into four groups. Most of the patients in the study group falls into Group 3 with a cholinesterase activity of 20% - 50%. Patients in Group 1 and Group 2 with very low serum cholinesterase activity had poor prognosis and it is statistically

significant (Table 28). According to a study conducted by Yun, HW and Lee, DH et al in China, they have concluded absence of increase in cholinesterase activity during the course of illness is associated with a poor outcome and serial measurements of cholinesterase gives a better guide to the treating Physician[112]. Nouira et al published that degree of poisoning and serum cholinesterase measured on admission has no prognostic value in predicting outcome[113]. But in our study the serum cholinesterase measured on the day of admission predicts the outcome with high statistical significance (Table 26, 28).

There are variations in changes of parameters considering with individual OP compounds involved in poisoning. In that Elevation in ALP, Change in Serum Sodium and fall in serum cholinesterase all turned out to be statistically significant (Table 29) when compared with the individual compounds.

Using intercorrelations between various parameter in this study the significance is noted in following parameters. A fall in serum cholinesterase is associated with rise in CPK, fall in serum cholinesterase is associated with a fall in serum potassium, and a fall in serum cholinesterase is associated with rise in AST and ALT (Table 30).

CONCLUSION

1. Organophosphorus poisoning is more common in adults of age group 20 – 30 years.
2. Incidence is high in male patients
3. Requirement of ventilator support is high, when the patient on admission has a higher grade of intoxication clinically (Using Bardin's grading)
4. Measurement of Serum potassium and serum cholinesterase is helpful in predicting the outcome and prognosis in OP poisoning. Hypokalaemia associated with reduced cholinesterase level is related with a negative outcome.
5. Increase in serum creatinekinase is commonly seen in organophosphate poisoning.
6. Increase in CPK MB and Troponin I is commonly seen in organophosphate poisoning because of the cardio toxicity involved in OP poisoning
7. CPK, CPK MB and Troponin I have high statistical significance to predict prognosis of the patient.
8. The significant increase of liver enzyme activity and serum amylase appears to correlate with clinical severity of the patient in OP poisoning.
9. Among the liver enzymes and serum amylase, ALT elevation has a statistical significance to predict the outcome of the patient.

LIMITATIONS

1. The period of study is minimal, huge data would have been collected if done for long time.
2. Study group is just adequate.
3. Serial estimation of the biochemical parameters during the course of hospital stay is not done.
4. Troponin I is done in qualitative method and not quantitative method.
5. Previously undiagnosed cardiac disease is not ruled out in the study patients.

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OPC POISONING CASE PROFORMA

NAME: AGE/SEX: DATE OF ADMISSION:

PLACE: COMPOUND:

MIXED WITH ALCOHOL:

QUANTITY:

TIME INTERVAL BETWEEN CONSUMPTION AND FIRST AID:

CHOLINERGIC SYMPTOMS:

BARDIN'S GRADE:

VENTILATORY ASSISSTANCE:

AST	
ALT	
ALP	
S. AMYLASE	
SODIUM	
POTASSIUM	
CPK	
CPK MB	
TROPONIN I	
S. CHOLINESTERASE	

ஆராய்ச்சி ஒப்புதல் கடிதம்

ஆராய்ச்சி தலைப்பு :

கி.ஆ.பெ.விஸ்வநாதம் அரசுமருத்துவக் கல்லூரி மற்றும் மகாத்மா காந்தி நினைவு அரசு மருத்துவமனை, திருச்சி பொதுமருத்துவப் பிரிவில்**பூச்சிக் கொல்லி விஷம்** அருந்தி நோயால் பாதிக்கப்பட்ட நோயாளிகளில் அவர்களுக்கு இந்நோயினால் ஏற்படும் விளைவுகளை முன்கூட்டியே அறியவும், நோயிலிருந்து சுகம் பெரும் வாய்ப்பு பற்றி அறிய இரத்தப் பரிசோதனையின் மூலம் அதற்கான காரணியை அளந்தறியும் ஆய்வு.

பெயர் : தேதி :

வயது : உள்நோயாளி எண் :

இனம் : ஆராய்ச்சி சேர்க்கை எண் :

இந்த ஆராய்ச்சியின் விவரங்களும் அதன் நோக்கமும் முழுமையாகவும் தெளிவாகவும் எனக்கு விளக்கப்பட்டது.

எனக்கு விளக்கப்பட்ட விஷயங்களை புரிந்துகொண்டு எனது சம்மதத்தை தெரிவிக்கிறேன்.

இந்த ஆராய்ச்சியில் பிறரின் நிர்பந்தமின்றி என் சொந்தவிருப்பத்தின் பேரில் பங்குபெறுகிறேன் மற்றும் இந்த ஆராய்ச்சியிலிருந்து எந்நேரமும் பின்வாங்கலாம் என்பதையும் அதனால் எந்தபாதிப்பும் ஏற்படாது என்பதையும் நான் புரிந்துகொண்டேன்.

இந்த ஆராய்ச்சியினால் ஏற்படும் நன்மைகள் பற்றி தெளிவாக மருத்துவர் மூலம் தெரிந்துகொண்டேன்.

நான் என்னுடைய சுயநினைவுடன் மற்றும் முழு சுதந்திரத்துடன் இந்த மருத்துவ ஆராய்ச்சியில் என்னை சேர்த்துக் கொள்ள சம்மதிக்கிறேன்.

ஆராய்ச்சியாளர் கையொப்பம் பங்கேற்பாளர் கையொப்பம்

நாள்:

இடம்:

K.A.P.VISWANATHAM GOVT. MEDICAL COLLEGE
TIRUCHIRAPALLI -1
INSTITUTIONAL ETHICS COMMITTEE

CERTIFICATE OF CLEARANCE

This is to certify that the project work titled Biochemical abnormalities in OPC poisoning and its prognostic significance proposed by Dr.L.Alen Binny part of fulfillment of M.D/M.S course in the subject of Medicine for the year 2014-2017 by The Tamilnadu Dr.MGR Medical University has been cleared by the Ethics committee.

1/7/2015

CHAIRMAN,
Institutional Ethics Committee
K.A.P.Viswanatham Govt. Medical College, Tiruchirapalli -1

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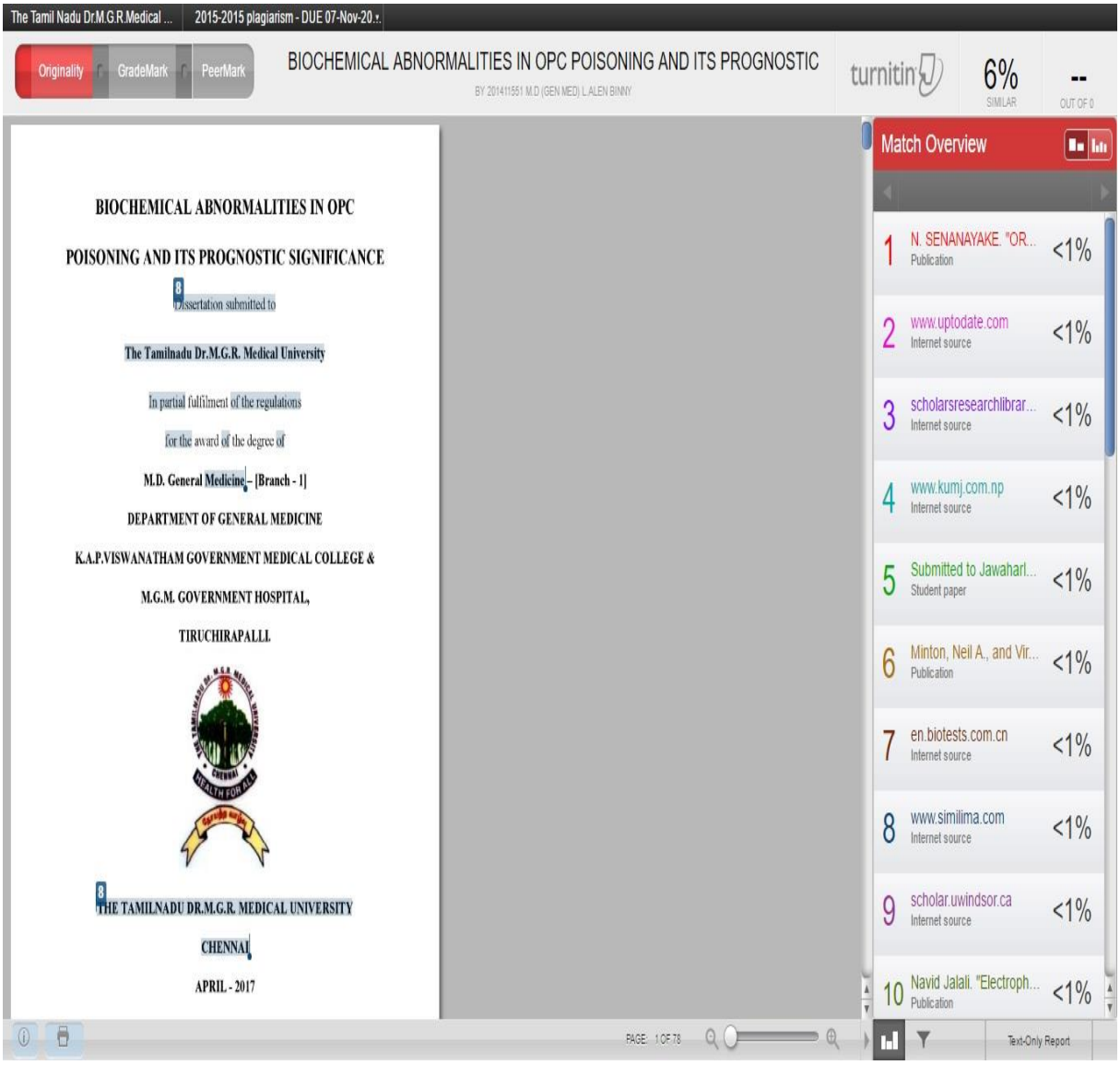

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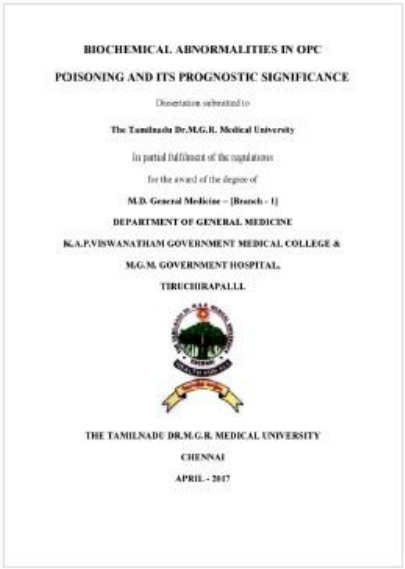

BIOCHEMICAL ABNORMALITIES IN OPC

POISONING AND ITS PROGNOSTIC SIGNIFICANCE

Dissertation submitted to

The Tamilnadu Dr.M.G.R. Medical University

In partial fulfilment of the regulations

for the award of the degree of

M.D. General Medicine – [Branch - I]

DEPARTMENT OF GENERAL MEDICINE

K.A.P.VISWANATHAM GOVERNMENT MEDICAL COLLEGE &

M.G.M. GOVERNMENT HOSPITAL,

TIRUCHIRAPALLI.

THE TAMILNADU DR.M.G.R. MEDICAL UNIVERSITY

CHENNAI

APRIL - 2017

MASTER CHART

GROUP	S. NO	AGE	SEX	COMPOUND	QUANTITY	ALCOHOL	TIME INT	SYMPTMS	BARDIN	VENTILATOR	AST	ALT	ALP	AMYLASE	SODIUM	POTASSIUM	CALCIUM	CPK	CPK-MB	S.AchE	TROP I	OUTCOME
1	1	23	F	PROFENOFOS 50%	50	N	2	Y	2	N	60	68	234	250	138	3	7.5	198	35	1175	0	1
1	2	47	M	FOLLIDOL	100	Y	2	Y	1	N	72	64	80	75	131	3.5	5.4	181	38	4944	0	1
1	3	30	M	FOLLIDOL	200	Y	3	Y	3	Y	109	128	95	83	135	3.4	8.1	155	108	422	1	0
1	4	27	M	DIMETHOATE 30%	200	Y	2	Y	2	N	69	28	250	88	143	3.5	8.1	86	23	2155	0	1
1	5	27	M	PROFENOFOS 50%	250	Y	3	Y	3	Y	120	134	320	315	132	3.4	10.6	2648	250	310	1	0
1	6	23	M	CHLORPYRIFOS 20%	150	Y	1	Y	3	Y	138	100	84	34	133	3.5	8.1	80	30	420	0	1
1	7	20	M	CARBOFURAN 3%	100	Y	6	Y	3	Y	187	132	106	213	132	3.1	8.2	3738	549	410	1	0
1	8	23	M	PROFENOFOS 50%	50	Y	6	Y	3	Y	137	140	135	55	139	3.4	7.4	85	66	879	1	0
1	9	60	M	TRIZOPHOS	150	Y	1	Y	3	Y	129	125	72	55	126	3.2	8.2	126	58	708	1	0
1	10	20	M	PROFENOFOS 50%	100	Y	4	Y	2	N	147	135	120	129	135	3.2	7.2	726	658	1313	1	0
1	11	40	m	profenofos 40%	200	N	2	Y	3	Y	120	18	88	44	132	3	7.9	30	23	802	0	1
1	12	23	F	PROFENOFOS 50%	150	N	3	Y	2	Y	172	150	265	280	135	3	7.2	298	135	1259	1	0
1	13	47	M	FOLLIDOL	100	Y	4	Y	2	N	170	150	81	74	131	3.5	5.4	181	65	3944	1	1
1	14	30	M	FOLLIDOL	180	Y	5	Y	3	Y	109	88	108	150	135	3	6.1	155	108	422	1	0
1	15	27	M	DIMETHOATE 30%	250	Y	3	Y	2	N	169	128	254	98	143	3	8.1	86	45	1155	0	1
1	16	27	M	PROFENOFOS 50%	250	Y	3	Y	3	Y	121	144	362	315	132	3.4	10.6	2648	250	310	1	0
1	17	23	M	CHLORPYRIFOS 20%	100	Y	2	Y	3	Y	138	117	184	234	133	3	8.1	180	80	520	0	1
1	18	20	F	PROFENOFOS 20%	100	Y	5	Y	3	Y	107	82	116	223	132	3.1	7.2	2738	758	410	1	0
1	19	23	M	PROFENOFOS 50%	80	Y	5	Y	3	Y	137	140	256	360	139	3.4	7.4	780	360	879	1	0
1	20	60	M	TRIZOPHOS	250	Y	1	Y	3	Y	29	220	72	55	129	3.2	8.2	326	190	708	1	0
1	21	20	F	PROFENOFOS 50%	100	Y	4	Y	2	N	47	35	120	129	135	3.2	7.2	726	658	1313	1	0
1	22	40	M	PROFENOFOS 50%	200	N	2	Y	2	N	20	18	88	44	132	3	7.9	30	23	802	0	1
1	23	23	M	FOLLIDOL	180	Y	2	Y	2	Y	85	59	108	215	135	3.4	7.8	1562	210	905	0	1
1	24	60	M	DIMETHOATE 30%	250	Y	2	Y	3	Y	78	76	95	142	138	3.6	7.6	2651	135	425	0	1
1	25	20	F	PROFENOFOS 50%	250	Y	3	Y	1	Y	85	64	74	128	134	3	8.1	120	56	3156	0	1
1	26	40	M	CHLORPYRIFOS 20%	100	Y	2	Y	2	N	140	157	180	249	134	3.1	7.9	1258	345	789	1	0
1	27	23	M	CARBOFURAN 3%	100	Y	3	Y	1	N	29	36	102	120	136	3.8	8.1	120	21	8569	0	1
1	28	47	M	PROFENOFOS 50%	80	Y	1	Y	2	Y	196	165	145	256	135	3	7.5	2156	209	1342	1	0
1	29	30	M	TRIZOPHOS	250	Y	6	Y	1	N	36	35	48	110	137	3.5	8.5	120	25	8562	0	1
1	30	27	M	PROFENOFOS 50%	100	N	4	Y	2	Y	220	198	215	352	135	2.6	7.5	980	450	1465	1	0
1	31	32	F	CHLORPYRIFOS 20%	100	N	2	Y	3	N	142	110	212	210	136	3.3	8.2	167	66	480	0	1
1	32	52	M	PROFENOFOS 50%	80	Y	1	Y	2	N	180	168	190	190	135	3.1	8.2	640	110	640	0	1
1	33	35	F	FOLLIDOL	150	N	4	Y	3	Y	100	120	90	140	134	3	5.8	160	100	500	1	0
1	34	40	M	CHLORPYRIFOS 20%	80	N	2	Y	3	Y	148	174	196	280	134	3	7.4	1390	420	590	1	1
1	35	24	M	DIMETHOATE 30%	200	Y	3	N	2	N	180	130	300	80	138	3.1	8	70	36	1980	0	1
1	36	30	M	PROFENOFOS 50%	100	Y	3	Y	2	Y	132	156	340	102	144	3.2	7.8	2450	248	1432	1	0
1	37	27	M	TRIZOPHOS	150	Y	4	Y	1	N	44	36	98	136	138	3.3	8.3	140	15	3960	0	1
1	38	20	F	FOLLIDOL	100	N	3	Y	2	N	155	130	106	84	134	3.2	5.8	160	90	2300	0	1
1	39	28	F	PROFENOFOS 50%	200	Y	3	Y	3	Y	64	98	128	240	134	3	8.8	860	520	950	1	0
1	40	36	M	PROFENOFOS 50%	100	N	2	Y	2	N	120	90	264	350	132	3.2	8.2	430	94	685	0	1
1	41	34	F	CARBOFURAN 3%	150	N	2	Y	1	Y	46	60	90	90	136	3.6	8.8	138	15	4980	0	1
1	42	45	M	FOLLIDOL	100	Y	2	Y	1	Y	140	156	268	120	134	3.1	7.9	130	45	2346	0	1
1	43	24	F	CHLORPYRIFOS 20%	200	N	4	Y	2	Y	120	98	240	130	132	3	7.6	2368	638	940	1	0
1	44	36	F	PROFENOFOS 50%	80	N	3	Y	1	N	34	28	120	90	140	3.6	8	260	40	460	0	1
1	45	28	M	PROFENOFOS 50%	150	N	2	Y	2	Y	134	180	260	130	135	3.2	7.2	148	62	980	0	1
1	46	23	M	DIMETHOATE 30%	100	Y	2	Y	2	N	47	80	120	93	135	3.3	8.8	158	36	980	0	1
1	47	52	M	PROFENOFOS 50%	200	Y	5	Y	1	Y	134	163	265	348	132	3.1	7.4	1482	340	3468	0	1
1	48	42	F	FOLLIDOL	200	N	4	Y	3	Y	186	130	234	140	134	3	9	1840	560	480	1	0
1	49	26	M	CHLORPYRIFOS 20%	100	Y	1	Y	1	N	96	120	160	110	136	3.2	8.4	980	96	3490	0	1
1	50	28	M	CHLORPYRIFOS 20%	120	Y	2	Y	1	N	106	135	120	105	138	3	8	956	90	3210	0	1

ABBREVIATIONS

OP- Organophosphates

CPK- Creatine phosphokinase

AST- Aspartate transaminase

ALT- Alanine transaminase

ALP- Alkaline phosphatase

SchE- Serum Cholinesterase

NTE- Neuropathy target esterase

FFP- Fresh frozen plasma

PON1- Paraoxonase 1

IMS- Intermediate syndrome