RANDOM BLOOD SUGAR LEVELS AND PSEUDO CHOLINESTERASE LEVELS THEIR RELEVANCE IN ORGANOPHOSPHORUS COMPOUND POISONING

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Abstract

Acetyl Cholinesterase in human beings, most cholinesterase in the nervous tissue and erythrocytes is acetylcholinesterase. [True ‘cholinesterase], whereas cholinesterase in the liver and plasma (or serum) is pseudocholinesterase

Most of the organophosphates used as the insecticides inhibit both pseudocholinesterase and acetylcholinesterase. Estimation of erythrocyte cholinesterase (acetylcholinesterase) is theoretically preferred, since it would indicate the degree of inhibition of synaptic cholinesterase (also acetylcholinesterase). Estimation of plasma cholinesterase (pseudocholinesterase) has an advantage because the measurement is simpler and more accurate than estimation of erythrocyte cholinesterase.

CHOLINESTERASE levels at birth are low (one fourth that of adults) but these levels increase rapidly reaching adult levels by second month of life.

In acute poisoning, manifestations generally occur only after more than 50% of serum cholinesterase is inhibited. The severity or manifestations parallels the degree of inhibition of serum cholinesterase action. Reduction of serum cholinesterase activity to 20-50% is considered as mild poisoning and less than 10% in severe poisoning in between 10 -20% moderate poisoning.

In severe poisoning, return to normal levels requires about four weeks for plasma cholinesterase and three weeks to several months for RBC cholinesterase when PAM is not administered.
Key Words

Random Blood Sugar Levels, Pseudo Cholinesterase Levels, Organophosphorus Compounds

**INTRODUCTION**

Since man started Agriculture he has been troubled by insects. He has been using insecticides since ages.

Organophosphorus and Organocarbamate compounds are used as agricultural and household insecticides and in the eradication of animal ectoparasites and human lice infestations. Of the various substances used for suicidal attempts in India. Organophosphates and Organocarbamates form a majority group.

Pesticides are easily available, cheap and can also be lethal. It makes them a common suicidal poison.

Some times poisoning may occur by accident.

Pesticides are a group of chemicals used for the destruction of organisms detrimental to man or his interests which include insecticides, Fungicides, Acaricides, Rodenticides, Herbicides and Fumigants.

Pesticides produce both acute and chronic poisoning.

Nerve gas agents like TABUN, SARIN, SOMAN are most lethal poisons and may be used in chemical warfare.

**HISTORY** \(^1,2\)

In 1820, LASSAIGNE First synthesized esters of phosphorus.
The German Chemist MICHAELIS developed a much more comprehensive understanding of the chemistry of organic phosphorus compounds.

Later in the career of Michaelis, A.E. ARBUZNOV in Russia conducted research on TRIVALENT PHOSPHOURUS COMPOUNDS, including the Michaelis-Arbuznov reaction to form the phosphorus-carbon bond.

ORGANOPHOSPHATES were introduced in 1854 but their toxicity was not known till 1931.

During the World War II, a comparatively new class of highly toxic chemical, THE ORGANOPHOSPHATES, was developed in 1937 chiefly by GERHARDSCHRADER OF I.G. FARBEN INDUSTRIE, first as agricultural insecticides and later as potential chemical warfare agents.

SCHRADER is credited with the 1944 discovery of the first marketed organophosphours pesticide, which contained “TETRAETHYL PYROPHOSPHATE” (TEPP) as its active ingredient.

DISOPROPYL FLUOROPHOSPHATE (DFP) was synthesized by SAUNDTERS.

SCHRADER NOTED the general formula for anti-cholinesterase organophosphorus compounds in 1937.

In 1950’s a series of Heterocyclic, Aromatic and naphthyl carbamates were synthesized, with a high, degree of selective toxicity against insects.
In INDIA, organophosphorus and organocarbamate compounds were introduced in 60’s and their toxicity reported in 1962.

WILSON and GINSBURG (1955) – Used pyridine-2-Aldoxime methyl chloride (2 PAM-Pralidoxime) – As choline-Esterase reactivator – for first time.

**Aim of the Study**

To study Clinical Profile of Organophosphorus Poisoning Cases admitted to Osmania General Hospital, covering clinical profile, Analysis of Random Blood Sugar levels, and estimation of Serum Pseudochoolinesterase levels at the time of admission and to correlate them with severity of Toxicity and predict the prognosis and mortality.

**MATERIALS**

The present study comprises of fifty cases of Organophsphorus poisoning directly admitted in Acute Medical Care of Osmania General Hospital, Hyderabad during a period from November 2013 to August 2015

**Inclusion criteria**

All cases of Organophsphorus poisoning admitted in Acute Medical Care of Osmania General Hospital, Hyderabad.
Exclusion criteria

1. Cases which are partially treated outside and referred later to Osmania General Hospital.
2. Intoxication with other chemicals like Organo Carbamate organochlorous compounds and Halobenzenes.
3. Patients with Diabetes, known alcoholics, diseases of liver and kidney, sepsis and known cases of Malignancy.

Various parameters studied were age and sex pattern, nature of the substance, clinical manifestations, Random Blood Sugar Analysis, Serum pseudocholinesterase levels, rental parameters, serum electrolytes, L.F.T. Electrocardiographic changes, therapeutic response and outcome of the cases.

METHODS

I. CLINICAL HISTORY

   (A) Nature of Exposure to Chemicals:

   - H/O Ingestion of the Poison
   - Type of the Poison
   - Amount of the Poison ingested
   - Time when the Poison was consumed
   - Identification of Empty Bottles brought to the Hospital by the Attendant
- H/O Exposure to Chemicals without Ingestion like
  
  i) Skin Contact
  
  ii) Inhalation
     a) Spraying
        o Power Sprayer
        o Ordinary Sprayer
     b) Direct Exposure

(B) Symptomatology


II. Clinical Examination :

(1) Level of Consciousness (2) Sweating (3) Smell (4) Pulse (5) Blood Pressure (6) Temperature (7) Respiratory Rate (8) Heart (9) Lungs (10) Pupils (11) Fasciculation

Results

Of the fifty cases studied 32 (64%) are males and remaining 18 (36%) are females. In our country, mostly men are bread winners of the family, being subjected to more financial problems. Secondly, spraying activities in the fields to a greater extent carried out by males than females. Thirdly,
alcoholism is more common in males, who may intoxicate themselves with insecticides in a state of confusion.

AGE INCIDENCE: The age of patients ranged from 18 – 60 years. A majority of patients (22 out of 50 – 44%) are in the age group 21 – 30 years.

TIME LAG: The time lapsed between the ingestion of insecticide and start of the therapy has a definite prognostic value. Those patients who delay hospitalization have moderate to severe symptoms. 36 out of 50 (72%) patients have presented to hospital within three hours. The minimal time lag is 35 min., maximum being 6 hours.

NATURE OF SUBSTANCE CONSUMED: Among the insecticides used as the intoxicant Quinol Phos was the most common agent used in 15 cases (26%) of patients followed by Chlorpyriphos the next common agent used in 11 cases (22%) as they are freely available in the market. Pesticides are commonly consumed by agricultural workers.

LEVEL OF CONSCIOUSNESS: Level of consciousness was altered in 52% of cases (drowsiness - 40%; semi consciousness 8%; unconsciousness - NIL %) Most of these insecticides have direct effect on the central nervous system.

PULSE: Holmstedt (1951) reported that Bradycardia is the earliest noticeable effect of cholinesterase inhibitors, but it was noted only in three case (6%), Bradycardia is the result of muscarinic manifestation of these
compounds. Tachycardia was recorded in 13 (26%) of cases, result of action on sympathetic ganglia. Normal pulse rate (60 to 100) was maintained in 68% of cases. Tachycardia may also be due to sympathetic discharge in response to hypotension.

**BLOOD PRESSURE:** Blood pressure was within normal range in 86% cases (Systolic 140 – 90 mmHg; Diastolic 90 – 60 mm Hg). Though theoretically hypotension is more common, in the study it was encountered in 4% cases only, whereas hypertension was seen in 10% cases. Similar findings were noted by other workers. Hypotension is due to action on medullary vasomotor centre of central nervous system, Hypertension is due to action on sympathetic ganglia, and secondary to fear an anxiety. No antihypertensive drug was administered in any instance and blood pressure returned to normal within 24 hours of hospitalization.

**SKIN TEMPERATURE:** Skin temperature was normal in 42% of cases; sweating with lowered skin temperature was observed in 58% of cases, as result of muscarinic manifestation.

**PULMONARY EDEMA:** Pulmonary edema was seen in 18% cases, which was effectively managed by oxygen and atropine.

**PUPILS:** The most significant and reliable diagnostic sign was the constriction of pupils, which was observed in 56% of cases.

**FASCICULATIONS:** Fasciculations, characteristic of cholinesterase inhibitor poisoning, were observed in 28% cases. They are muscle twitchings caused due to stimulation of Nicotinic receptors at neuromuscular junctions and indicate moderate to severe toxicity.
RANDOM BLOOD SUGAR LEVEL: Random Blood Sugar levels were estimated for all the cases, levels of more than 140 mg. per dl were found in 13 (26%) cases of which 6 (12%) cases had more than 200 mg. per dl. Hyperglycemia in Anticholinestearse inhibition is transient and has been attributed to stimulation of nicotine receptors present on sympathetic ganglia leading to increased release of catecholamines from adrenal medulla (Tareg 35 at al 2001). Hyperglycemia in Anticholinesterase poisoning usually is seen in cases of severe poisoning.

ESTIMATION OF SERUM PSEUDOCHOLINESTERASE: In this study depression of serum pseudocholinesterase levels directly correlating with severity of poisoning. Out of fifty patients 13 (26%) of the patients had mild depression of serum pseudocholinesterase levels and 21 (42%) of patients had moderate depression of serum cholinesterase levels and 16 (32%) of patients showed severe depressions of cholinesterase levels.

In severe depression of serum pseudocholinesterase cases mortality rate was high 9 out of 16 (56.25%) due to respiratory paralysis, in moderate depression mortality rate was 4 out of 21 (19.5%). All other cases with moderate and mild depression survived.

MORTALITY: Thirteen out of fifty patients expired during the treatment. Respiratory paralysis was the cause of death in all 13 cases. Four out of 13 deaths occurred on first day, five on the second day, three on the third day and one on fourth day.
DISCUSSION

In the present study of fifty cases of Organophosphorus compound poisoning studied at Osmania general hospital 64% were males and the age group 21-30 yrs was more commonly affected with 44% of patients falling in this age group.

The findings were in concordance with Agarwal S.B. et al series 41 in which 190 patients from two hospitals in Ahmedabad were studied which showed male preponderance of 63%.

Similar findings were noted in the studies conducted by other workers, D.G.Gunnur 40 et al series (Males 54.8%) which was a study conducted in Gulburga region in 923 cases over a period of five years. Majority of patients (45.6%) were in 21-30 yrs of age.

In D Gohel et al series 42 in which 100 cases were studied male patients were 60% and patients falling in 21-30 yrs age group were 39%.

In majority of cases the cause of poisoning was suicidal intention and route of poisoning was by ingestion. The circumstances which force people to take this drastic step are mainly due to broken love affairs, marital disharmony, failure in examination, unemployment and financial problems, which are more common in young age.

The time lapsed between the ingestion of insecticide and start of the therapy has a definite prognostic value. In our study 72% of patients have presented to hospital within three hours. The minimal time lag was 35 min., maximum being 6 hours.
These findings were similar to V.N.Dhadke\textsuperscript{45} et al study that included 50 cases admitted at Dr.V.M.Medical college, Solapur in which 80% of the patients presented with in 6 hrs.

In D.G.Gunnur\textsuperscript{40} et al series the time lapse was 3-4 hrs in 19% of cases which is in contrast to our study. This might have occurred due to long distances of referral hospitals from the rural areas.

Patients presented with wide variety of symptoms of which nausea and salivation were most commonly observed in 82% and 62% of the cases respectively.

Our findings were in concordance with Agarwal S.B. et al series ie, nausea in 82.1% and salivation in 61.1% of the cases. Similar results with nausea in 79.2% and salivation in 70.1% were found in D.G.Gunnur\textsuperscript{40} et al series.

In the present study, altered consciousness was found in 52% of the cases which correlated to observations made by Agarwal S.B. et al ie, 44.2% but was in contrast to the results of 17% observed by D.G.Gunnur et al.

Other symptoms like dysnoea, and bladder and bowel incontinence were observed in 28% and 32% respectively.

In our study it was observed that Bradycardia was present in 6% of cases and Tachycardia was recorded in 26% of cases.

In observations made by Agarwal SB et al with Bradycardia was present in 6.3% and Tachycardia in 25.3%. In a study done in 47 cases at School of Medicine, Erciyes University, Kayseri, Turkey by Murat Sungur\textsuperscript{39} et al it was observed that Bradycardia was present in 2.3% and Tachycardia
was present in 25% of the cases. Both these studies are in concordance with the findings of the present study.

In our study the Blood Pressure was within normal range in 86% cases (Systolic 140 – 90 mmHg; Diastolic – 90 – 60 mm Hg). Though theoretically hypotension is more common, in the study it was encountered in 4% cases only, whereas hypertension was seen in 10% cases. Similar findings were noted by other workers like S.B.Agarwal et al, hypertension in 10.6%.

Pulmonary edema was seen in 18% cases in our study. The findings were similar to those observed by D.Gohel et al (18%) and in 24% of cases in a study conducted by A.P.N.Kumar et al on 100 cases at Nizam’s Institute of Medical Sciences, Hyderabad.

The most significant and reliable diagnostic sign was the constriction of pupils, which was observed in 56% of cases in our study. The findings were in concordance with Agarwal SB et al series in which miosis was observed in 64.2% of the cases. Similar findings with miosis in 42% of the cases was observed by D.Gohel et al.

Fasciculations which are nicotinic manifestations characteristic of cholinesterase inhibitor poisoning were observed in 28% cases in our study. Similar observations were made by D.Gohel et al and VN Dhadke et al with 29% and 26% respectively.

Electrocardiography recordings were traced in all the cases. Normal ECG was recorded in 70%. Other changes observed were sinus bradycardia 6% and sinus tachycardia 26%. The findings were in concordance with S.B.Agarwal et al series sinus tachycardia 25.3%, sinus bradycardia 6.3%
and T wave inversions 6.3%. It was recorded by D.Gohel et al abnormal ECG 56% with sinus tachycardia 20%, sinus bradycardia 28%, VPCS 5% VT 1% QT interval Prolongation 1% and AV Block 1%.

Random Blood Sugar levels were estimated for all the cases, levels of more than 140 mg. per dl were found in 26% of the cases of which 12% of the cases had more than 200 mg. per dl. Of the 6 cases who had RBS levels > 200 mg / dl 4 cases died, all the four patients had depressed serum pseudocholinesterase levels. In patients with Hyperglycemia more than 200 mg / dl at admission pseudocholinesterase levels were severely depressed and mortality was correlating with the levels of Hyperglycemia. It has been described in text book of Toxicology by Thomas J. Haley, William O. Berndt that there is a period of transient hyperglycemia that correlates with severity of poisoning in cases of Organophosphorus poisoning due to stimulation of nicotinic receptors on adrenal medulla. In our study Hyperglycemia more than 200 mg / dl at admission was associated with mortality in 8% of cases

Hyperglycemia was observed in 30% of the cases by DS Rao et al in a study conducted on 30 patients at SVRRGG Hospital and SVIMMS, Tirupati, similar observations of 20% of cases with Hyperglycemia were made by APN Kumar et al.

B.Jayaprakash et al who studied 100 patients at Vijayanagar Institute of Medical Sciences, Bellary wherein Hyperglycemia of more than 200 mg / dl was correlated with decreased pseudocholinesterase levels and mortality. Hyperglycemia associated with decreased pseudocholinesterase levels and increased mortality was observed in 10% of the cases.
In this study depression of serum pseudocholinesterase levels directly correlating with severity of poisoning. Out of fifty patients 26% of the patients had mild depression of serum pseudocholinesterase levels and 42% of patients had moderate depression of serum cholinesterase levels and 32% of patients showed severe depressions of cholinesterase levels.

Similar observations were made by SD Zawar et al in a study conducted at Indira Gandhi Medical College, Nagpur in 37 patients, mild depression of serum Pseudocholinesterase levels was seen in 30%, moderate depression in 20% and severe depression in 50% of the cases.

Mortality rates of 26% were observed in our study, 6% of the patients required ventilatory support and two patients (4%) developed Intermediate syndrome. Respiratory paralysis was the major cause of death. This was in concordance with D.Gohel et al series in which mortality was 30%. The mortality observed in V.N.Dhadke et al series was 16%. The difference in the mortality rates may be due to early intervention in V.N.Dhadke et al series.
CONCLUSIONS

1. Hyperglycemia is commonly observed in cases of Organophosphorus poisoning

2. Hyperglycemia is seen in cases with moderate to severe poisoning

3. Hyperglycemia at admission correlates with depression of Pseudocholinesterase levels in Organophosphorus poisoning.

4. Random Blood Sugar levels of > 200 mg / dl at admission and depression in Pseudocholinesterase levels < 1000 U/L ( p < 0.005) are reliable parameters to predict mortality and ventilator requirement in Organophosphorus poisoning.
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