Significance of Serum Cholinesterase Levels in Patients of Organophosphorus Poisoning

Venkateshwarlu N.[1*], Gandiah P.[2], Prabhakar K. K.[3], Indira G.[4], Sivarajappa P.[5]

[1,4,5]Professor, [2]Professor and Head of department, [3]Assistant Professor

Department of General Medicine,SVS Medical College, Mahabubnagar Andhra Pradesh, INDIA

Corresponding Address:

venkatatreya@gmail.com

Research Article

Abstract: Organophosphourus Poisoning (OP) is very important and challenging to treat in clinical situation. It carries a large amount of mortality and morbidity along with much economic loss to our society particularly the poor and farming community as most of our economy depends on crops. Early recognition clinically and biochemically guided management of the cases is the need of hour. One hundred cases of OP poisoning were analyzed. The severity was accessed clinically and by serial estimation of serum cholinesterase levels. Most of our patients had severe poisoning requiring mechanical ventilation; atropine and PAM (Prolidoxime) form the main stay of treatment. Good nursing care apart from medicines and artificial ventilation is needed for speedy recovery of the ailment. Serum cholinesterase depression is a good indicator for severity and diagnosis of the disease though improvement in levels of it may not be to the extent of that of clinical improvement.

Key words: Organophosphorus Poisoning, Serum Cholinesterase levels.

Introduction

Organophosphorus Compounds are used as agricultural and household insecticides and in the eradication of animal ectoparasites and human lice infestation. Of the various substances used for suicidal attempts in India, Organophosphates, Organochlorides and Carbamates form a majority group. They are common agents of suicidal and accidental poisoning, as a result of their ready availability, cheap and easy accessibility. Several hundred people around the world die each year from organophosphorous poisoning, especially in developing countries [1]. WHO estimates that three million cases of poisoning occur worldwide, mostly in the developing countries[2] Diagnosis of organophosphorus poisoning (OPP) is a) based upon the history given by the patient / attendants, b) based upon clinical examination (signs on presentation), c) gastric fluid analysis, and d) measurement of serum cholinesterase levels. Nigg HN, Knak [3] opined blood cholinesterase levels as human bio markers of organophosphorous pesticide exposure.

Materials and Methods

This study presents 200 consecutive cases admitted to acute medical care of S.V.S Hospital, with history of ingestion of insecticidal organophosphorous compounds between 1-1-2008 and 31-12-2010 were taken up for the study. The study of these patients consisted of detailed history regarding the (a) Quantity of ingestion, (b) Time of interval between ingestion and hospital admission. The true cholinesterase and pseudo cholinesterase enzymatic estimations were done calorimetrically. And for all the cases Hemoglobin level and Liver Function Test was estimated. Estimation of serum cholinesterase is by Kinetic Method. Samples were collected from the patient at admission, on 3rd day, 7th, 14th days and on 45th day

Observations of Clinical Data

All cases were analyzed well by the scientific committee and tabulated for easy understanding as following. 30 cases were below the age of 20 yrs. 96 patients' fall between ages of 31 and 40. The youngest in this study was 13 yr old while the oldest was 60 yrs of age.

Table 1: Showing number of patients in various age groups

Years	Male	Female	Total
10-20	12	18	30
21-30	38	58	96
31-40	40	28	68
41-60	4	2	6
Total	94	106	200

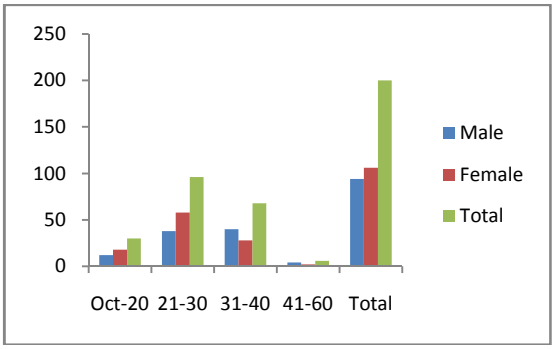


***Figure 1*:** Showing number of patients in various age groups

Table 2: Showing various clinical symptoms

Symptom	Percentage
Nausea and Vomitting	88
Miosis	80
Sweating or Salivation	56
Fasciculation	52
Pulmonary Edima	40
Abdominal Pain	38
Techycardia	31
Hypotonia	22
Coma	22
Hypotension	16
Diarrehoea	9
Bradycardia	9

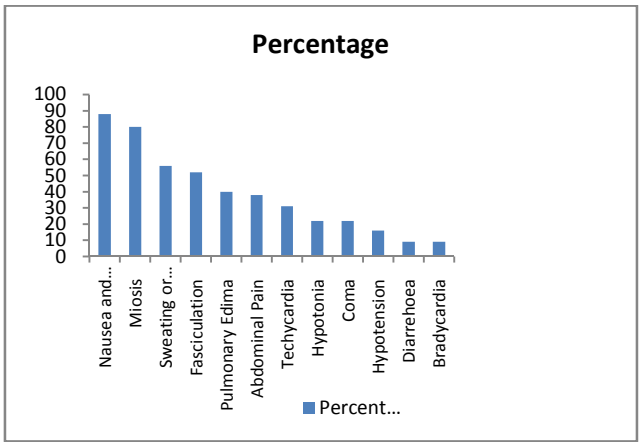


Figure 2: Showing various clinical symptoms

Table 3: Depicting the Clinical Severity

Severity	Number
Mild	16
Moderate	34
Severe	50

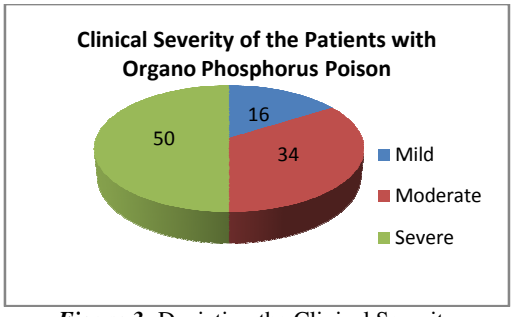


Figure 3: Depicting the Clinical Severity

Serum cholinesterase levels roughly represent the severity of clinical classification of the disease. The following table and pictoral representation highlights the same fact.

Table 4: Showing the levels of Serum Cholineasterase as against the severity

Serum Cholinesterase	Levels
Mild	2240
Moderate	1640
Severe	1008

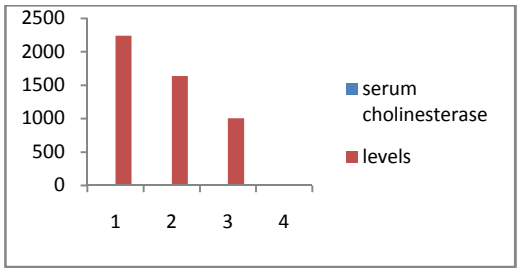


Figure 4: Showing the levels of Serum Cholineasterase as against the severity

The same (serum cholinesterase levels) is represented in terms of percent of depression of serum cholinesterase activity in mild, moderate and severe cases.

Table 5: Showing the depression of serum cholinesterase

Clinical severity	Percentage
Mild	42
Moderate	64
Severe	76

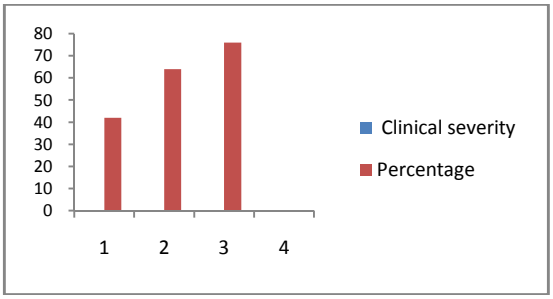


Figure 5: Showing the depression of serum cholinesterase

Table 6: Complications of OP poisoning in our series

Complications	Number
Expired	22
Pulmonary Edema	46
Aspiration Pneumonia	25
Convulsions and Coma	19
Intermediate Syndrome	18
Total	130

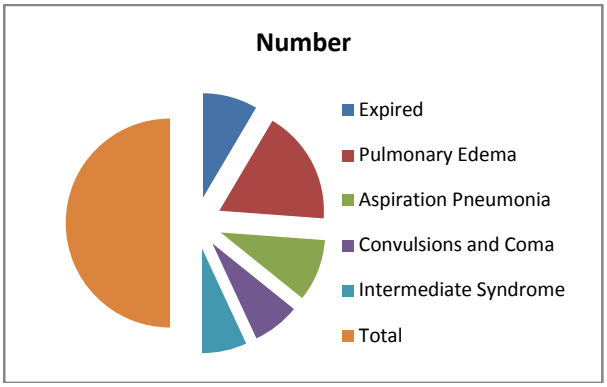


***Figure 6*:** Complications of OP poisoning in our series (pie diagram)

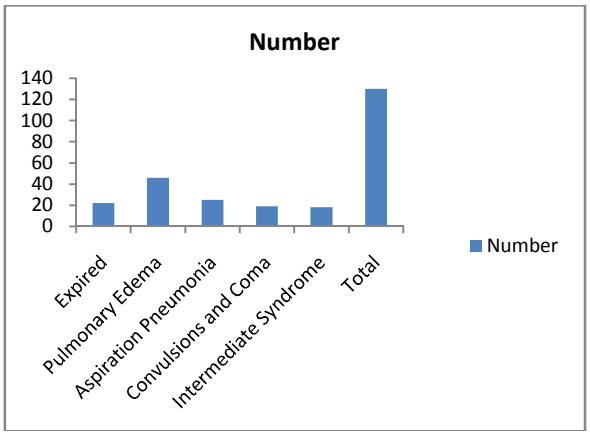


Figure 7: Complications of OP poisoning in our series (graphic representation)

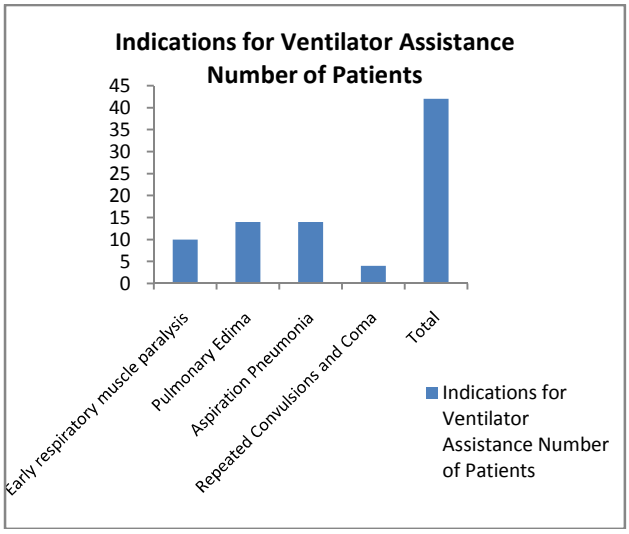
Complications

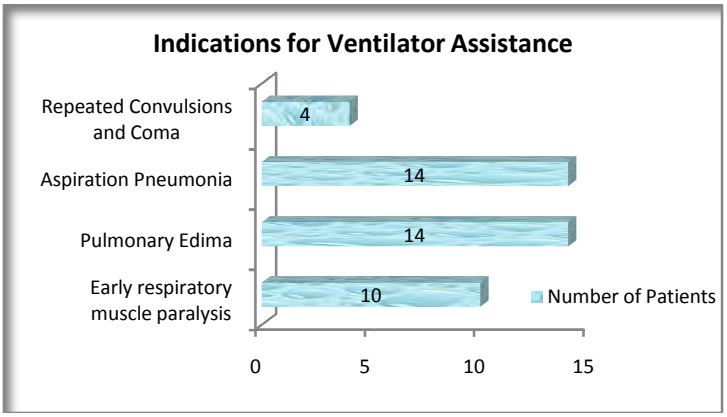
Serious complications encountered in our study are as follows:

A total of 22 patients expired within 48 hours of admission, 46 patients developed pulmonary edema , 25 patients developed aspiration pneumonia, 19 patients developed convulsions while 18 cases developed intermediate syndrome. A total 42 cases needed artificial ventilation; 14 cases of pulmonary edema, 10 cases had early respiratory muscle weakness , 14 were of aspiration pneumonia and 4 patients of repeated convulsions needed mechanical ventilation.

Indications for Ventilator Assistance

Ventilator Assistance	Number of Patients
Early respiratory muscle paralysis	10
Pulmonary Edima	14
Aspiration Pneumonia	14
Repeated Convulsions and Coma	4
Total	42

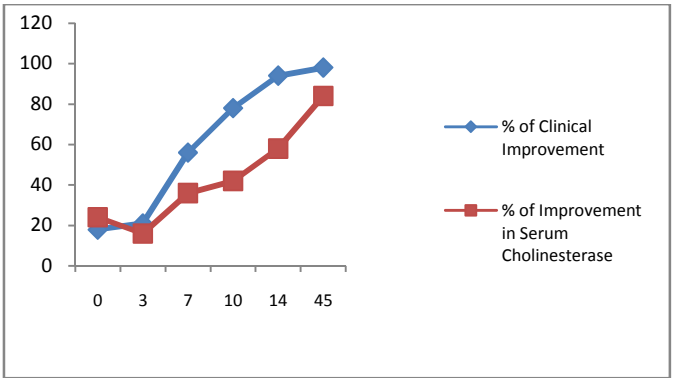




All the 178 patients recovered fully clinically initially in about 10-14 days . the patients were followed upto minimum of 2 months (though our study restrict to 6 weeks) but biochemically at the end of 14 days there was only 58% improvement, while clinically 94% improvement was observed . Improvement of 98 % clinically and 84 % biochemically was observed in our study.

Serial Estimations of Serum-Cholinesterase with respect to clinical improvement

Days	% of Clinical Improvement	% of Improvement in Serum Cholinesterase
0	18	24
3	21	16
7	56	36
10	78	42
14	94	58
45	98	84



Discussion

Organophosphorous poisoning in recent years has become the commonest source for most of the suicidal cases. Increase in stress because of unemployment, poverty and conflicting relationships in young couples. Females were found to be more vulnerable to self-poisoning. Deliberate self-harm by suicidal poisoning is common all over the world. Poisons most commonly used vary in different geographical regions. In our Hospital, these constituted for more than

92% of the cases. Similar reports have been published by Ganapathi and Janaki *et al* in 1962 and Narayana Reddy in 1974. They are most probably preferred because of ready availability, rapid action and poor knowledge of lethal potency. Several factors have been implicated as responsible for the severity of organophosphorous poisoning like dose of poison ingested, the compound and the time lapse before the start of treatment.

Assessing clinical severity by cholinesterase activity:

Serum cholinesterase has correlation with clinical picture [5]. In MILD it was 32.7% activity in moderate it was 20.3% and in severe it was 9.4%. This was in fact correlating with the classification given by Namba *et al* [4] in which mild was 20 – 50% moderate 11 – 20% and severe 0 – 10%. However such correlation was also found with erythrocyte cholinesterase activity.

Table 7: Comparing the depression of serum cholinesterase levels of present study with that of Namba *et al*[4]

	Present study	Namba *et al*
Mild	16 %	20-50%
Moderate	34 %	11-20%
Severe	50 %	8-10%

Assessment of progress & Prognosis by cholinesterase

Serum cholinesterase activity is found to be more sensitive is found to be more sensitive indicator in assessment of clinical progress and prognosis of given cases 6. In no case was there a spontaneous rise of activity of cholinesterase as patient recovered. In all cases serum cholinesterase levels fell by first 24 – 48 hours before it started rising. It is known that after a delay of 36 hours, the enzyme alteration is irreversible. Inhibition even after recovery from symptoms was a feature in some of the cases. Cholinesterase of the synapse seems to recover far more rapidly than blood cholinesterase. RBC and Serum cholinesterase levels did not show any improvement in the first week despite marked clinical improvement in the present study. This fact was reported in other studies too [7,8,9]. Organophosphates do not accumulate in tissues, but a cumulative esterase's since these enzymes severe as Buffers, protecting the cholinesterase of the synapse. In patient who expired there was no recovery in both RBC, plasma cholinesterase activity this point could not be confirmed as the patients expired quite early. Serum cholinesterase recovery was very slow. In most of cases it started rising after 48 – 86 hours but recovery was not as rapid as RBC cholinesterase. The rise in the serum cholinesterases is statistically significant from the 7th day by the p value which is less than 0.1. Atropine and Pralidoxime therapy aided by serum cholinesterase affords excellent prognosis. If adequate atropinisation is maintained for at least 24 hours after the rising levels of cholinesterase activity, to summarize serum cholinesterase indicates the effectiveness of therapy with PAM. Serum cholinesterase indicates the prior presence of cholinesterase inhibition even after the recovery clinically. Present study demonstrates long time to reach normal levels. It is shown by several investigators that, there is not a single clinical diagnostic feature which would be constantly present in this condition. Serial levels of cholinesterase levels are needed to confirm the diagnosis. As the initial sample may be on the higher levels in particular the serum cholinesterase level, as is evident by other studies [10]. In the present study, serum CHE activity was estimated in all cases, it was lowered below 70% of normal and was found to be a constant biochemical feature. A correlation was found between CHE activity and clinical severity initially and further decline occurs up to 72 hrs before the levels start improving. However, level below 70% is definitely abnormal and should strongly suggest possibility of ingestion of insecticidal organophosphorous compound. Thus this investigation forms a diagnostic laboratory finding. This was reported in earlier studies too[3]. Estimation of RBC cholinesterase levels are relatively cumbersome and tedious, and at times it is difficult to get actual values in one sitting, may have to be repeated as against serum cholinesterase levels which is easier to perform and reproduce. The following chart demonstrates more depression of serum cholinesterase activity in severe cases as compared with that of mild ones.

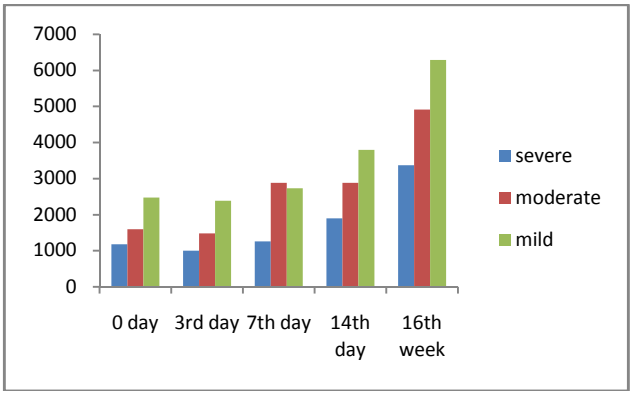


Figure 7: Serum Cholinesterase Levels During The Course Of Treatment

Conclusions

A total of 200 cases of organophosphorous poisoning were studied aged between 13 and 60 years. Abdominal pain, nausea, vomiting, giddiness, oronasal secretions were common symptoms and meiosis was a common sign. The Serum cholinesterase activity was estimated in all the cases and was found to be lowered in all below 70% of normal on acute presentation. The investigations were repeated on 3rd day, 7th day, 14th day, and at 6th week thereafter. The active substance in the entire insecticide organophosphorous compound is

Diazinon. This compound inhibits cholinesterase by phosphorylation and lowers the level of active cholinesterase. A total of 22 patients expired within 24 hours of admission, 46 patients developed pulmonary edema requiring artificial ventilation, 25 patients developed aspiration pneumonia, and 19 patients developed convulsions. In the present series the serum cholinesterase activity was estimated, and it was lowered below 70%, and such decrease should suspect acute poisoning. It is predominantly seen in young people of both sexes between 15 – 35 years of age group more in male population. The time interval between the ingestion of poison and the treatment is directly proportional to the severity. All patients who recovered showed rising levels of serum cholinesterase. The rise of serum cholinesterase did not correlate with the clinical recovery of the patient. In all the twelve patients who expired, there were low values of serum cholinesterase activity. Atropine and PAM therapy, the serum cholinesterase levels have guided in the prognosis. In a given case following PAM administration the serum cholinesterase indicates the effectiveness of PAM and serum cholinesterase indicates the prior presence of the cholinesterase inhibition even after recovery of the RBC cholinesterase. RBC cholinesterase levels estimation is cumbersome, poor reproducibility, expensive than estimation of Serum cholinesterase. We found that the significance of serum cholinesterase levels estimation were equally useful in diagnosing organophosphorous poisoning. Moreover, the test for serum cholinesterase is quite simple and does not require elaborate equipment and is readily available, where as the test for RBC cholinesterase is cumbersome and tedious and requires expertise for performing the test.

References

1. Eddleston M, Patterns and Problems of delobrate self poisoning in the developing world. QJM 2000: 93:715-31
2. Jeyaratnam J, Acute pesticide poisoning, a major health problem. Worls Health Stat Q 1990:43:139-45.
3. Nigg HN, Knaak JB: Rev Environ Contam Toxicol. 2000;163:29-111. Blood cholinesterases as human biomarkers of organophosphorus pesticide exposure.
4. Reddy KSN. The Essential of Forensic Medicine and Toxicology. 28th ed. Hyderabad: Om Sai Graphics; 2009. p. 427-31.
5. Namba, T. (1971). "Cholinesterase inhibition by organophosphorus compounds and its clinical effects." Bulletin of the World Health Organization 44 (1): 289-307.
6. Pandya TP,Srijithessh PR Srivastva SB, Dabhi As Brahmbhatt BK, Thorat PB. RBC cholinesterase And serum cholinesterase in organophosphorus Poisoning. (Abstract). J Assoc physicians India 2003; 51: 1199
7. Bobba R, Venkataraman BV, Pais P, Joseph T. Bobba R, Venkataraman BV, Pais P, Joseph T. Correlation between the severity of symptoms in organophosphorus poisoning and cholinesterase activity (RBC and plasma) in humans.
8. Yamanaka S, Yoshida M, Yamamura Y, Nishimura M, Takaesu Y: Nippon Eiseigaku Zasshi. 1993 Dec;48(5):955-65. [A study on acute organophosphorus poisoning--changes in the activity and isoenzyme patterns of serum cholinesterase in human poisoning]
9. Brahmi N, Mokline A, Kouraichi N, Ghorbel H, Blel Y, Thabet H, Hedhili A, Amamou M: Am J Emerg Med. 2006 Nov;24(7):822-7. Prognostic value of human erythrocyte acetyl cholinesterase in acute organophosphate poisoning.
10. Midtling JE, Barnett PG, Coye MJ, Velasco AR, Romero P, Clements CL, O'Malley MA, Tobin MW, Rose TG, Monosson IH. West J Med. 1985 Apr;142(4):514-8. Clinical management of field worker organophosphate poisoning.