Relation between Serum Cholinesterase and Mortality among Patients with OP Poisoning

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Abstract

Introduction: Serum cholinesterase levels can indicate the prior presence of cholinesterase inhibition even after recovery of acetyl cholinesterase activity by pralidoxime in organophosphorus poisoning. In acute poisoning, manifestations generally occur only after more than 50% of cholinesterase is inhibited.

Methodology: 36 patients presenting with history of Organo-phosphorus poisoning and feature of respiratory failure (requiring ventilatory support) were included in the present study.

Results: In the present study 27% were died.

Conclusion: Higher mortality was seen patients having mild suppression of SCE activity.

Key words: Acetylcholinesterase, OP poisoning, Mortality

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Introduction

Estimation of acetyl cholinesterase level in circulation is theoretically preferred in organophosphorus poisoning since it would reflect the degree of inhibition of synaptic cholinesterase at motor end plates. But, in practice, estimation of serum cholinesterase has an advantage because the measurement is simpler and more accurate than estimation of the acetylcholinesterase. Serum cholinesterase levels can indicate the prior presence of cholinesterase inhibition even after recovery of acetylcholinesterase activity by pralidoxime in organophosphorus poisoning.[1] In acute poisoning, manifestations generally occur only after more than 50% of cholinesterase is inhibited. The severity of manifestation parallels the degree of inhibition of serum cholinesterase (SCE) activity pertinently only in initial stages.T2 The normal values range between 5100 to 11700 IU / Ltr. According to Proudfoot,[2] the Organophosphorus poisoning may be classified based on the levels of serum cholinesterase (SCE.) on presentation as follows : ■ In mild poisoning: SCE. level is 20 - 50 % of normal ■ In moderate poisoning: SCE. level is 10 - 20 % of normal ■ In severe poisoning: SCE. level is < 10 % of normal In severe poisoning, return of normal levels requires above 4 weeks for serumcholinesterase and about 10 to 12 weeks for acetyl cholinesterase. Acetyl cholinesterase regenerates at approximately 1% per day, whereas serum cholinesterase regenerates at a more rapid rate, at approximately 25% in the first 7-10 days. The confirmation of diagnosis depends on demonstrating reduced cholinesterase activity in the circulating blood. Activity is expressed as percentage of normality of healthy adults. Values above 80% normality imply that no significant absorption has taken place. There is no specific upper limit, cases with values between 50% and 80% are usually symptomless but indicate a slight absorption. Early effects, mainly abdominal discomfort and cold sweats may occur at 20% - 30% of normality. Severe cases would be expected to have very low serum cholinesterase activity in the blood, for example 5-10% but some apparently severe cases of parathion poisoning have had up to 50% normal values, while some cases of over exposure, with serum cholinesterase levels reduced to 5 % normality, have proved symptomless.

Normal values of serum cholinesterase are widely variable from one person to another as well as in the same individual at different times. 1. Low serum cholinesterase levels have been observed in some disease states and may also be genetically determined. 2. Following pralidoxime administration, true cholinesterase levels indicate the effectiveness of PAM and serumcholinesterase levels indicates prior presence of cholinesterase inhibition even after recovery of true cholinesterase activity by PAM, hence the latter cannot be used to assess the effectiveness of PAM therapy. 3. Serumcholinesterase level at a particular time in the blood is not constant but continuously changing as the inhibition of the enzyme by inhibitors and spontaneous reactivation will take place simultaneously

Methodology

The study was conducted at the Respiratory Intensive Care Unit of Department of Anaesthesiology. 36 patients presenting with history of Organo-phosphorus poisoning and features of respiratory failure (requiring ventilatory support) were included in the present study. Prior approval for the study and the protocol was obtained from the institution ethical committee. After explaining the possible prognosis in the course of organophosphorus poisoning, consent from a responsible attendant / informant of the patient was obtained before the actual study was initiated.

Inclusion Criteria for the study were as follows:

1. Provisional diagnosis of organophosphorus poisoning in a patient irrespective of age / sex, based on history by attenders.
2. Clinical features suggestive of severe grade of organophosphorus poisoning with clinical evidence of respiratory insufficiency.

Exclusion Criteria for the study were as follows:

1. Patients with double insecticide / multiple poisoning with other drugs such as opioids, diazepam, barbiturate etc.,
2. Patients with history of respiratory diseases like bronchial asthma, cardiac diseases, neuromuscular diseases like myasthenia gravis or muscular dystrophy or other concomitant illnesses.

Each of the patients with Organophosphorus poisoning were assessed clinically with detailed history and thorough physical examination.

Features correlating to: (a) Severity of organophosphorus poisoning and (b) Respiratory failure (to identify those requiring mechanical ventilation) were assessed.

(a) Criteria for diagnosis of severe grade of organophosphorus poisoning: 25

■ Unconsciousness ■ Marked miosis ■ Loss of pupillary reflex to light ■ Muscular fasciculation ■ Flaccid paralysis ■ Excessive secretions from mouth and nose ■ Crepitations ■ Respiratory distress

(b) Criteria for diagnosis of respiratory failure : -The patients who have features suggestive of severe poisoning as stated above are then assessed for ventilatory support based on following: ■ Apnoea ■ Obvious Hypoventilation ■ Persistent Cyanosis inspite of 02 supplementation ■ Persistent Tachypnoea - Respiratory rate (per minute) > 24 ■ Persistent Sp02 < 90% with Oxygen supplementation by non invasive means. ■ Active involvement of accessory muscles of respiration.

Immediately after clinical assessment, blood samples were sent for investigations including Haemoglobin level , Total count and Differential Blood Count (DC), ESR, Blood sugar, blood urea, serum creatinine, serum electrolytes and Serum Cholinesterase level (More investigations as necessary were done after institution of treatment and ventilation).

Immediate Management: Patients were given stomach wash, body wash and intravenous cannulation done. Injection PAM, bolus dose — 1 gm. I.V. and Inj. Atropine bolus 5-10 mg. IV were given. Patients were reassessed for respiratory. failure, and if so, intubated and shifted to Respiratory Intensive Care unit by Ambu ventilation.

On arrival in the Respiratory Intensive Care Unit, the patients were immediately connected to ventilator and supportive therapy was also initiated along with definitive therapy.

The Definitive Therapy for Organophosphorus poisoning: Protocol followed in our unit was: - Inj Atropine Infusion 25-50 mg. / 24 hrs, with 1 mg bolus IV every 2nd hrly as and when required, till signs of atropiniiation appeared. - Inj PAM infusion at 50 - 100 mg / hr administered for the initial 72 hrs. depending upon the severity.(following the initial bolus 1 gm. given on arrival at emergency ward)

Supportive Therapy (as required): ■ Maintenance of intravascular volume by IV fluids. ■ Antibiotics to prevent and treat infections. ■ Inotropic support for cardiac function. ■ Regular and thorough endotracheal and oral suction. ■ Chest physiotherapy. ■ Nutritional support by enteral feeding when indicated. ■ Measures to reduce gastric acidity and secretions.

Ventilator Management: The patients were put on Drager Savina ventilator with the following initial settings-Mode - SIMV with pressure support Tidal volume - 7-10 ml/kg body wt Respiratory rate - 10-12 bpm Fi02 -0.4-0.6 I : E ratio - 1 : Pressure support - 10-15 cm H2O initially and gradually reduced to 0 with recovery . PEEP - 2 to 5 cm H2O increments was used as indicated

Weaning Technique — Consisted of SIMV with PS • CPAP T-Piece

Investigations: Repeat and / or additional investigations as required by the patient's status were ordered and Serum Cholinesterase estimation was repeated on the 3rd, 5th, 7th, 9th and 11th day of stay in the Respiratory Intensive Care Unit.

Serum cholinesterase: The reference values and Interpretations / definitions are as follows:

The serum cholinesterase activity was measured by kinetic/ DGKC calorimetric method, of Zydus Pathline Limited. EDTA samples are sent to the laboratory.

The results are expressed in KU / L which is U / L x 1000. The laboratory reference range used in the present study for serum cholinesterase: 5100 to 11700 IU / Ltr. Based on the Serum Cholinesterase values, the severity of poisoning may be defined as per (Proudfoot classification) 22 with above normal range:

■ Mild poisoning: SCE. level 20 - 50 % of normal / > 2001 IU / L ■ Moderate poisoning: SCE. level 10 - 20

% of normal /1001 -2000 IU / L ■ Severe poisoning: SCE. level is < 10 % of normal / < 1000 IU / L

Results

Majority of the patients of poisoning in our study (80%) were below 40 years of age. The youngest patient was 12 years old and the oldest 68 years. Out of 36 patients included in the study 64% were males and remaining 36% were females.

Table 1: Relation between initial levels of Serum cholinesterase and Mortality

Range of SCE (IU/L)	Severity	Frequency	Mortality
<1000	Severe	02 (06%)	0
1001 – 2000	Moderate	06 (17%)	01 (17%)
2001 – 3000	Mild	16 (44%)	05 (31%)
3001 – 4000	Mild	08 (22%)	03 (37%)
4001 – 5000	Mild	01 (03%)	0
>5000	Mild	03 (08%)	01 (33%)
Total		36 (100%)	

In the present study 27% were died. Higher mortality was seen patients having mild suppression of SCE activity. The least rates were in the <1000 IU/L of SCE (0%) and 1001 – 2000 IU/L of SCE (17%) groups.

Table 2: Mortality and trend of SCE levels

Days	1	3	5	7	9	11
SCE levels (IU/L)	2780.60	2242.10	2707.50	3090.57	2833.2	3005.6
P value		NS	NS	NS	NS	NS

NS – Nothing significant

This table gives the changing values of SCE in the group of patients who died, from the day of admission till death. There is a fall by third day with improvement and stabilization over the subsequent days. These changes are not however statistically significant but clinically significant.

Discussion

In those with first day values of > 3000 IU / L of SCE, the serial estimation showed an increase in SCE levels on 3rd day and then largely stabilizing over the next six days. In the set of patients who presented with 1000 to 3000 IU / L of SCE, there was no improvement in the levels upto 3 days after presentation, indicating continuing suppression with lower levels of SCE at presentation. There has been no such serial estimation over 11 days in other studies even though this has been done in three individual cases by Suvit Areekul et al.[3]

We estimated the average change in the SCE levels comparing with first days readings with the subsequent days (till 11th day), as applicable. We found that there was a maximum improvement in the SCE levels on the 3rd day — about 66 %. We also found that there was increase, albeit at lesser rates, in the subsequent days as well.(The SCE levels increased from the day of admission: 3065.57 ± 384.65 IU / L, reaching 3349.14 ± 222.57 IU / L on the day weaning was started to 3648 .33 ± 247.96 IU / L on the day of successful weaning). Lee P, Tai DY,[4] studied 23 adults with OP poisoning and found that the threshold levels of SCE for successful weaning from mechanical ventilation was 2900 IU / L.

G. Avasthi, G. Singh,[5] while prospectively evaluating 29 patients of OP poisoning clinically along with SCE estimation found that clinically detectable respiratory muscle weakness could be found in all patients with severely depressed values but could still occur at any level of SCE.

There was a mortality rate of 27 % in our study, with no relation to SCE levels : Highest mortality was seen (37%) in patients with SCE levels of 60-80% of normal value and also lower mortality being observed (17%) in patients with SCE levels of 40% of normal values, hence there is no correlation between mortality and SCE level suppression. Mehta et al.,[6] reported similar patterns in their study wherein two patients with severe suppression (values of < 10 % SCE) could survive. J. Sunder Ram et al.[7] observed a mortality of 8 % (4 out of 45), with no correlation with SCE values. A. Dua et al[8] (433 studied 43 patients of OP poisoning and found that neither the mortalities nor the clinical severity correlate with SCE levels. This indicates that there is no relation between mortality and the trends of changes in levels of SCE.

Conclusion

The levels of SCE did not change significantly over the days the patients were admitted and managed in the respiratory unit and died with no fixed trend as well.

Conflict of Interest: None

Source of Support: Nil

References

1. Narayan Reddy K. S. The Essentials of Forensic Medicine and Toxicology 2004. 23rd Edt Pg. 415-417.
2. PROUDFOOT. A: Organophosphate and carbamate insecticides in diagnosis and management of Acute poisoning 1st Edition Oxford Blackwell Scientific 1982:153 — 7.
3. Suvit Areekul et.al .Serum and red cell cholinesterase activity in people exposed to organophosphate insecticide South east Asian Journal. TROP. MED.PUB.HLTH 1981: 12: 94 — 95.
4. Lee P, Tai D.Y. Clinical features of patients with acute organophosphate poisoning requiring intensive care. Intensive care medicine. 2001; 27(4): 694 — 699.
5. G.Avasthi, G .Singh .Serial Neuro- electrophysiological studies in acute organophosphate poisoning - correlation with clinical findings, serum cholinesterase levels and atropine dosage JAPI 2000; 48; 794 — 799.
6. Mehta A.B et al. clinical features and plasma acetylcholinesterase activity in poisoning with insecticidal organophosphorus compounds.
7. J.Sunder Ram et al: Continuous infusion of high doses of atropine in the management of organophosphorus compound poisoning JAPI 1991: 39: 190 — 193.
8. A .Dua et al serum cholinesterase levels in organophosphorus poisoning- does it Predict Mortality? JAPI 2001: 49: 168 – 169.