



Research Article

JMR 2018; 4(5): 219-222

September- October

ISSN: 2395-7565

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www.medicinarticle.com

Received: 11-08-2018

Accepted: 06-10-2018

A Study of Serum Cholinesterase Activity with Clinical Correlation in Patients with Acute Organophosphorous Poisoning

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Abstract

Background: Organophosphorus (OP) compounds acts by inhibiting cholinesterase activity. Estimation of serum AChE levels is done to assess the severity of OP poisoning. This study was planned to evaluate the correlation between the level of serum AChE enzyme and the clinical outcome so that the findings can be used for management of these critical patients. **Material and methods:** A prospective study was conducted on 100 patients with OP compound poisoning. Serum AChE levels were estimated in all patients before administration of any treatment. Patients were classified into 4 grades of severity of poisoning as per the Namba et al. criteria and were treated accordingly. **Results:** Serum AChE level in patients with the latent grade of poisoning was 5643.76 ± 1627.83 IU/L, in patients with a mild grade of poisoning was 3178.8 ± 530.30 IU/L, in patients with moderate grade of poisoning was 2360 ± 273.12 IU/L and in the severe grade of poisoning was 521.68 ± 288.8 IU/L. Out of 48 patients with latent grade of poisoning 91.66% recovered. In a moderate grade of poisoning, 50% recovered while 30% died and with severe grade of poisoning 32.43% patients recovered while 51.35% patients died. **Conclusion:** Estimation of serum AChE level on admission act as a good tool to predict the prognosis of the patient as low levels of serum AChE are associated with bad prognosis and higher chances of mortality.

Keywords: Organophosphorus, Cholinesterase, Acetylcholinesterase, Poisoning.

INTRODUCTION

Organophosphorus (OP) compounds are the most commonly used pesticides worldwide and poisoning due to these compounds had become the major public health problem specially in developing countries.^[1] Though, World Health Organisation (WHO) had estimated that around 3 million people die every year due to various poisonings, the actual incidence of organophosphate poisoning is difficult to find out. It is estimated to be around 2,50,000 to 3,50,000 deaths per year globally.^[2-4]

Being an agricultural country, OP compounds are used abundantly in India for farming purpose. As these compounds are cheaper and easily available over the counter, its indiscriminate use and therefore handling and storage has increased leading to an increase in a number of poisoning cases. The incidence of OP poisoning in India is among the highest in the world.^[5, 6] Recent data from National Crime Bureau shows that suicide by consuming pesticides account for approximately 19% of all cases of poisoning related deaths in India and various reports suggested that, the rate of suicidal poisoning with OP compounds ranges from 10 to 43%. Most of the reported cases are in young adults specially females, farmers and from low strata.^[7-9]

The morbidity and mortality in OP poisoning cases are high and survival critically depends upon the severity of poisoning and initiation of treatment. Considering the availability of limited resources, it is important that treatment prioritization should be made depending on the severity of poisoning as all patients cannot always be managed in ICUs due to low resource Indian setups.^[10] Hence, it is pertinent that the severity of poisoning needs to be ascertained based on either clinical or laboratory assessment

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As OP compounds act by inhibiting both cholinesterase and pseudocholinesterase activities^[11] irreversibly and fact that this leads to accumulation of acetylcholine at synapses causing overstimulation of acetylcholine receptors and disruption of neurotransmission in both central and peripheral nervous systems, it is reasonable to estimate serum AChE levels to assess the severity of OP poisoning.^[12, 13] With this rationale, we plan a study to evaluate the correlation between the level of serum acetylcholinesterase enzyme and the clinical outcome so that the findings can be used for the management of these critical patients.

MATERIALS AND METHODS

This was a prospective study conducted on 100 patients who had OP compound poisoning and brought to the casualty of tertiary care, referral centre, DUPMC, Jalgaon over the period of 2 years. The study was approved by the Institutional Ethics Committee and a verbal consent to include the patients in the study was obtained from the immediate relatives of the patient. The cases were diagnosed from the history of OP compound consumption as indicated by patients/relatives/referring doctor and/or signs and symptoms of OP poisoning and/or compound brought by patient's relatives.

Patients were classified into 4 grades of severity of poisoning as per the Namba et al. criteria.^[11] (1) Latent if there are no clinical manifestations and serum AChE activity is inhibited by 10 to 50%, (2) Mild if there are some clinical manifestations and serum AChE is 20 to 50% of normal value, (3) Moderate if there are clinical manifestations and serum AChE is 10 to 20% of normal value and (4) Severe if there are marked clinical manifestations and serum AChE is less than 10% of normal value.

At the time of admission, thorough clinical examination was carried out and investigations were done that included complete blood count, renal function tests, liver function tests, chest X-ray, electrocardiogram, arterial blood gas analysis and urine analysis. Serum AChE levels were estimated in all patients before administration of any treatment by the kinetic/DGKC calorimetric method.

Treatment: All patients had thorough stomach wash. Their clothes were removed, and the body was cleaned to avoid further absorption from the skin. Patients with respiratory failure were intubated and ventilator support was given.

Patients were treated initially with IV atropine (2-3 mg bolus). Atropine was repeated every 5-15 minutes depending on the severity of poisoning until signs of atropinization were observed. Drying up of secretions were taken as the sign of atropinization. Heart rate was maintained at the rate of 120 beats/mins. Continuous infusion was given when there was an improvement in parameters or whenever large doses of atropine were required (to maintain atropinization). The rate of continuous infusion was maintained at a constant value by means of the infusion pump. This helps in calculating the total amount of atropine given in 24 hours.

Pralidoxime was given only to patients who had consumed OP compounds and was not given to patients with organocarbamate compounds poisoning. Patients initially received 2 gm of pralidoxime (Inj. P₂AM) IV stat and 2.5/5 gms were given in 5% Dextrose Normal Saline (DNS) pint (5 pints in 24 hours i.e. 12.5/25 gms of Inj. P₂AM in 24hours) via continuous IV drip.

In some patients, IV diazepam was given to prevent restlessness and broad-spectrum antibiotic was given to the majority of patients considering the possibility of aspiration pneumonia due to excessive retching and vomiting. In 21 out of 100 patient's serum AChE levels were normal and hence P₂AM and atropine therapy was not required in them.

Statistical analysis

All the data was collected and entered into the excel sheet. Quantitative data (eg: demographic data: age, gender etc.) were expressed in Mean and Standard deviation. Qualitative data (eg: hospital stay etc.) was expressed in Number and frequency. The p values <0.05 were considered as statistically significant. Statistical analysis was performed using the SPSS statistics version 17.0.

RESULTS

A total of 100 patients were evaluated in this study. Mean age of patients was 32.57 years (range 16-75 years); out of this 66% were male and 34% were female. 64% of these patients belong to young age group (20 to 40 years), 12% middle age group (40 to 50 years) 11% young age (10 to 20) and 3 to 5% above 50 years age group. As per the Namba et al. criteria,^[11] 48% patients suffered latent poisoning, 5% mild, 10% moderate and 37% suffered severe poisoning. Detailed demographics are given in Table 1. In most of these patient's classical signs of OP poisoning were observed. In patients with severe poisoning, GI symptoms, excess secretions, bradycardia, respiratory distress and fasciculations was seen. Miosis was observed in those cases who were not subjected to treatment elsewhere.

Table 1: Characteristics of patients (n=100)

Parameters	Values n (%)	
Gender		
Male	66 (66%)	
Female	34 (34%)	
Age group	Male	Female
10-19	6 (9.09%)	5 (14.70%)
20-29	24 (36.36%)	15 (44.11%)
30-39	19 (28.78%)	6 (17.64%)
40-49	7 (10.60%)	5 (14.70%)
50-59	4 (6.06%)	1 (2.94%)
60-69	4 (6.06%)	1 (2.94%)
70-79	2 (3.03%)	1 (2.94%)
Total	66 (66%)	34 (34%)
Grade of severity		
Latent	48 (48%)	
Mild	5 (5%)	
Moderate	10 (10%)	
Severe	37 (37%)	
Outcomes of patients		
Recovered	66 (66%)	
Expired	22 (22%)	
DAMA	12 (12%)	
Total	100 (100%)	
Patients on ventilator support		
Recovered	8 (20.5%)	
Expired	22 (56.4%)	
DAMA	9 (23.1%)	
Total	39 (100%)	
Average values of serum AChE (IU/L)		
Latent	5643.76 ± 1627.83	
Mild	3178.80 ± 530.30	
Moderate	2360.00 ± 273.12	
Severe	521.68 ± 288.8	
Average stay (days)		
Latent	6 ± 3.81	
Mild	8.80 ± 1.48	
Moderate	10.30 ± 5.29	
Severe	13.15 ± 7.3	
Average age (yrs)		
Expired	36.45 ± 10.50	
Recovered	29.20 ± 12.40	
Average serum AChE (IU/L)		
Expired	1448.82 ± 617.50	
Recovered	5149.68 ± 2392.23	

The average hospital stay in all studied patients was 9.22 ± 6.31 days (range 1 to 30 days). It was longer in severe poisoning cases 13.15 ± 7.3 days and shorter in latent poisoning cases 6 ± 3.81 days. Out of the 100 studied patients, 66% recovered fully, 22% died and 12% took discharge against medical advice and were not traceable.

Cholinesterase levels

When serum AChE level was categorized as per grade of poisoning it was seen that, mean serum AChE level in patients with the latent grade of poisoning was 5643.76 ± 1627.83 IU/L, in patients with mild grade of poisoning was 3178.8 ± 530.30 IU/L, in patients with moderate grade of poisoning was 2360 ± 273.12 IU/L and in severe grade of poisoning was 521.68 ± 288.8 IU/L. (Table 2)

Table 2: Average level of serum AChE and outcome of patient in each grade of severity

Clinical Severity	Total cases	Average serum AChE level IU/L	Recovered	Expired	DAMA
			No. (%)	No. (%)	No. (%)
Latent	48	5643.76 ± 1627.83	44 (91.66)	0 (0)	4 (8.34)
Mild	5	3178.80 ± 530.30	5 (100)	0 (0)	0 (0)
Moderate	10	2360.00 ± 273.12	5 (50)	3 (30)	2 (20)
Severe	37	521.68 ± 288.8	12 (32.43)	19 (51.35)	6 (16.22)

When we evaluate the patient's outcome as compare to grade of poisoning it was observed that, out of 48 patients with latent grade of poisoning 91.66% recovered and other went DAMA, in patients with mild grade of poisoning all patients recovered, in patients with moderate grade of poisoning 50% recovered while 30% died. And in patients with severe grade of poisoning 32.43% patients recovered while 51.35% patients died. Mean serum AChE levels in patients who died (in all grades of poisoning) were 1448.82 ± 617.50 IU/L and 5149.68 ± 2392.23 IU/L in those who recovered. (Table 1)

Total 39 patients were put on the ventilatory support within 24 hrs of admission due to respiratory failure and the mean serum AChE levels in them were 1640.49 ± 1645.63 IU/L and in those who do not require ventilator support was 5610.92 ± 2519.76 IU/L. Out of these 39 patients 56% patients died, 21% recovered and 23% took discharge against medical advice. In patients who do not require ventilatory support 95% recovered and 5% took discharge against medical advice. (Table 3)

Table 3: Average serum AChE and outcome of the patients those on ventilator and not on ventilator

Status of the patient	No. of patient	Average serum AChE (IU/L)	Outcome		
			Expired	Recovered	DAMA
			No. (%)	No. (%)	No. (%)
On ventilator	39	1640.49 ± 1645.63	22 (56.40)	8 (20.50)	9 (23.10)
Not on ventilator	61	5610.92 ± 2519.76	0 (0)	58 (95.08)	3 (4.92)

DISCUSSION

In the present study, it was observed that most patients had consumed the OP compounds with suicidal intention and the reason for this was failed love affairs and quarrel with parents over studies. As majority of the studied strata were from low income group and uneducated or

both; unemployment, ill-literacy, decreased threshold of day-to-day problems and failure in examinations acts as a triggering factor in them for committing suicides. Most important reasons for this is easy availability and inexpensiveness of OP compounds.^[14, 15] Cypermethrin, chlorpyrifos and dichlorvos formed the mainstay among the OP compounds that were used for poisoning.

Most of our study population (64%) belongs to young age group of 20 to 40 years. This finding is in line with other published studies whose studied population belong to young age groups. Males were more vulnerable to poisoning in this study and this finding was in line with some studies where male sex had predominated. But when we took a good look of a literature it was observed that female sex shows more preponderance to poisoning. Thus, our study suggests strong association between young age and acute poisoning cases. Predominance of male population in study clearly suggest distress in them because of economic burden and unemployment.

Gastrointestinal symptoms were common presentation in most of the earlier studies and an observation of this study was also in concordance with them. Other reported symptoms were fasciculation's and increased secretions.

Overall mortality with OP compounds in our study was 22%. This was slightly higher than that observed in other studies.^[16, 17, 19-21] Out of 22% patients who died in this study 86.36% (19 patients) belong to severe poisoning group and 13.64% (3 patients) belong to moderate poisoning group. This indicated that even moderate degree poisoning can lead to mortality. Deaths was mostly due to the respiratory failure as a consequence of central respiratory depression, respiratory muscle weakness, and/or direct pulmonary effects (bronchospasm and bronchorrhoea).^[22] Complications of pre-hospital respiratory arrest and unconsciousness, such as aspiration and anoxic brain damage, cause further deaths in the patients.

Other factors that could have played a role in mortality after OP poisoning include presence of co-morbid conditions or inadvertently stoppage of atropine infusion particularly at night in the wards or not getting the exact amount of poison consumed or exact time at which the poison was consumed. Also, it was observed that approximate duration between consumption and arrival at the hospital varied from less than 1 hour to a maximum of 12 hours with majority of subjects reached the hospital within 6 hours of consumption of poison. In this study we observed that as the grade of poisoning increases more was the depression in serum AChE levels. The patients who had history of ingestion but were asymptomatic had an average serum AChE level of 5643.76 IU/L and those with severe poisoning had an average serum AChE level of 521.68 IU/L and required treatment in excess of 12 days. Thus, the association between clinical picture after OP poisoning and serum AChE levels was seen to be fairly accurate in assessing the severity of the poisoning and predicting the outcome at the time of admission. This helps in management and treatment of patients. Even, the average value of serum AChE on admission in the patient who died was much lower 1448.82 ± 617.50 IU/L than that in the recovered group 5149.68 ± 2392.23 IU/L.

There was also an association between serum AChE levels and duration of hospital stay. More the depression in the serum AChE levels, more prolong was the hospital stay. It was also observed that mechanical respiratory support was required in the management of severely poisoned patients whose serum AChE levels were depressed thus establishing good correlation between these two parameters. All these finding were supported by other authors findings.^[16-18]

In patients who had enzyme levels less than 1000 IU/L (severe poisoning group), prognosis was ominous, and they were prone to sudden death inspite of aggressive therapy and clinical improvement. Reasons for this can be sudden release of fat soluble

organophosphates from adipose depots leading to critical inhibition of enzymatic activity and sudden circulatory collapse and hypotension incompatible with life.

We considered estimation of serum AChE at the time of admission. As serial estimation is usually done to confirm the diagnosis only when the initial value is normal and clinical symptoms do not correlate well with the estimated value, the absence of serial estimation has less likely had an effect on the outcome of the patients in our study. Also, the exact duration between consumption of poison and arrival at hospital was not reported and it was as per the relative's narration.

CONCLUSION

Thus, we conclude that OP compounds poisoning is highly fatal and hence it requires early diagnosis and proper management including ventilatory support. Estimation of serum AChE level on admission act as a good tool to predict the prognosis of the patient as low levels of serum AChE are associated with bad prognosis and higher chances of mortality.

Acknowledgment

Authors are grateful to Medicine Department, Dr Ulhas Patil Medical College, Jalgaon for their assistance during evaluation of patients.

Conflict of Interest

The author(s) declare no conflict of interests.

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