Relation of Serum Cholinesterase with Clinical Severity and Treatment Outcomes of Organophosphorus Poisoning in a Tertiary Care Center, a Prospective Observational Study

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ABSTRACT

Introduction: Acute organophosphorus (OP) pesticide poisoning is widespread and is the most common poisoning in many developing countries and vary in different geographic regions. Organophosphorus compounds are anti acetylcholinesterase's which exert their toxicity by interfering with the normal function of acetylcholine. So the present study was done to assess the serum cholinesterase levels correlation with clinical severity to determine the treatment outcome (Need for mechanical ventilation and mortality).

Material and methods: A cross-sectional study was conducted among 100 patients admitted with OPC poisoning in the department of general medicine, Velammal Medical College Hospital and Research Institute, Madurai from January 2016 to July 2019. The diagnosis was made based on history or evidence of exposure to OP compound within 24 hours; Clinical severity was assessed and categorized according to POP scale. Serum Cholinesterase values were defined as per Proudfoot classification. IBM SPSS version 22 was used for statistical analysis.

Results: OP poisoning predominantly affected males in the age group 21 to 40 years. The majority had a moderate grade of poisoning with Serum cholinesterase levels between 2001 to 5000 (IU/l). In this study, the mortality was 25%, and 40% of patients had to be ventilated. There was no statistically significant relationship between age, gender, clinical severity, time-lapse, Serum cholinesterase levels, mortality with mechanical ventilation. Mortality rate showed a statistically significant relation with clinical severity ($p<0.001$).

Conclusion: Clinical severity was associated with treatment outcomes. No particular trend of the association was observed between clinical severity and serum cholinesterase levels. Serum cholinesterase levels had shown no association with outcomes

Keywords: Clinical severity, Organophosphorus, Poisoning, Serum Cholinesterase

INTRODUCTION

Acute organophosphorus (OP) pesticide poisoning is widespread and is the most common poisoning in many developing countries and vary in different geographic regions.[1] Accidental and occupational exposures were estimated to cause 1 million cases with 200,000 deaths.[2] Recent data from the National crime bureau of India shows a mortality rate of 26.6% (34,869) in the year 2017 by consumption of pesticides. Accidental Intake of Insecticides was reported among 1403 males, 812 females in the age group of 18 -30 years. The majority of suicides were reported in Maharashtra (17,646) followed by 14,459 suicides in Tamil Nadu, 12,014 suicides in West Bengal.[3] Poisoning is the fourth most common cause of mortality in rural India. In North India aluminium phosphide and organophosphate, poison is common. Aluminium phosphide or organophosphate, these substances were developed to control insects and pests and have become major contributors in the causation of poisoning death.[4]

Organophosphorus compounds are anti acetylcholinesterase which exert their toxicity by interfering with the normal function of acetylcholine, an essential neurotransmitter throughout the autonomic and central nervous system. OP acts by inhibiting the enzyme cholinesterase, results in accumulation of acetylcholine at synapses and myoneural junction leading to cholinergic overactivity.[5] The manifestations of toxicity are a result of this effect, affecting the patient's physiology. The anticholinesterase effects can be evidenced biochemically by suppression in the serum levels of serum cholinesterase and of red cell cholinesterase. Previous studies associating the severity or prognosis of Organophosphorus poisoning with an estimation of serum cholinesterase have been contradictory. According to the study Senayeke et al[6] serum cholinesterase level is depressed after OP poisoning. The Peradeniya Organophosphorus Poisoning scale assesses the severity of poisoning based on the symptoms at presentation and is simple to use. Noiura S et al[7] reported that serum cholinesterase levels have no prognostic value in acute OP poisoning.

Owing to the limited availability of resources, all OP poisoning patients are not managed in ICUs in the Indian setup. So the present study was done to assess the serum cholinesterase level, and it's a correlation with clinical severity among

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cases of organophosphate poisoning. Secondly, to determine the treatment outcome (Need for mechanical ventilation and mortality) and analyze the factors associated with treatment outcome among the OP poisoning cases.

MATERIAL AND METHODS

A cross-sectional study was conducted among 100 patients with OPC poisoning in the department of general medicine, Velammal Medical College Hospital and Research Institute, Madurai from January 2016 to July 2019. Prior approval for the study and the protocol was obtained from the institutional ethical committee. Informed consent was obtained from the patient's attendant. All patients in whom a provisional diagnosis of OPC poisoning was made based on the patient's clinical presentation/history as recorded from the patient's attendant/details of poison containers were included in the study.

Multiple compound/tablet poisoning, contradictory diagnosis regarding the compound, patients with a history of bronchial asthma/cardiac illness or neuromuscular diseases, Patients who died within few minutes of hospitalization even before the initial treatment could be given were excluded from the study.

A detailed case history was taken as per the proforma, general physical examination and systemic examination was done soon after admission. Laboratory investigations such as Complete blood count, Random blood sugar, Renal function test, Liver function test, were done at the time of admission. The patients were monitored regularly until the outcome.

Clinical severity was assessed and categorized according to POP scale. A score of 0 to 3 is considered as mild poisoning, 4 to 7 as moderate poisoning and 8 to 11 as severe poisoning.[6] The score was obtained at initial presentation before any medical intervention, and it represented the muscarinic, nicotinic and central effects of the acute cholinergic manifestations of OP poisoning.

Serum cholinesterase was measured by kinetic/DGKC calorimetric method using EDTA samples. 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) with above normal range:[8]

- 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

Qualitative variables were gender, serum cholinesterase levels, clinical severity grade. Quantitative variables include age. The major outcome variable is the severity of poisoning. P value of less than 0.05 is considered a statistically significant value. IBM SPSS version 22 was used for statistical analysis.[9]

RESULTS

A total of 100 subjects were included in the final analysis. Majority of (66%) participants w were aged between 21 to 40 years, followed by 41 to 60 years (23%), < 20 years 9 (9%) and >60 years was (2%). Males constituted 80% of the study population fiftieth(58%) participants had clinical grade II, 25 (25%) participants had grade I, I 17(17%) participants and I had clinical-grade I poisoning. Time-lapses between consumption and reporting to the hospital was 61 to 180 minutes in 51% of the subjects. The lapse was 181 to 300 minutes in 21% and > 300 minutes in 6% of subjects. Only 17% reached in < 60 minutes to the hospital. Six (6%) participants had serum cholinesterase level <1000 (IU/l), in 18 (18%) subjects it was 1001 to 2000 (IU/l), in 68(68%) subjects it was 2001 to 5000 (IU/l) and 8 (8%) subjects had >5000 (IU/l). Among the study population, 40 (40%)

Parameters	Number (%)
Age group	
<20	9(9%)
21-40	66(66%)
41-60	23(23%)
>60	2(2%)
Gender	
Male	80(80%)
Female	20(20%)
Clinical severity grade	
I	17(17%)
II	58(58%)
III	25(25%)
Time-lapses duration in minutes	
<60	17(17%)
61-180	51(51%)
181-300	26(26%)
>300	6(6%)
Serum cholinesterase level (IU/l)	
<1000	6(6%)
1001-2000	18(18%)
2001-5000	68(68%)
>5000	8(8%)
Mortality	
Yes	25 (25%)
No	75 (75%)
Mechanical ventilation	
Yes	40 (40%)
No	60 (60%)

Table-1: Summary of baseline characteristics (N=100)

(Serum Cholinesterase Level (Iu/L)	Clinical Severity		
	Grade 1 (N=17)	Grade 2 (N=58)	Grade 3 (N=25)
<1000	0 (0%)	5 (8.62%)	1 (4%)
1000 To 2000	2 (11.76%)	12 (20.69%)	4 (16%)
2000 To 5000	13 (76.47%)	35 (60.34%)	20 (80%)
> 5000	2 (11.76%)	6 (10.34%)	0 (0%)
*No statistical test was applied- due to 0 subjects in the cells			

Table-2: Correlation between clinical severity and serum choline esterase levels

subjects needed mechanical ventilation, and 25 (25%) met with mortality. (table 1)

When the association between clinical severity and serum choline esterase levels was assessed, no particular trend was observed. But as compared to grade 1, a higher proportion of subjects with clinical-grade 2 & 3 had shown lower levels

Parameters	Study group		Chi square	P value
	Mechanical ventilation (N=40)	No Mechanical ventilation (N=60)		
Age group				
<20	1 (2.5%)	8 (13.33%)	*	*
21-40	22 (55%)	44 (73.33%)		
41-60	15 (37.5%)	8 (13.33%)		
>60	2 (5%)	0 (0%)		
Gender				
Male	38 (95%)	42 (70%)	9.375	0.002
Female	2 (5%)	18 (30%)		
Clinical severity				
grade I	1 (2.5%)	16 (26.67%)	*	*
grade II	14 (35%)	44 (73.33%)		
grade III	25 (62.5%)	0 (0%)		
Time lapse duration in minutes				
<60	8 (20%)	9 (15%)	2.869	0.412
61-180	23 (57.5%)	28 (46.67%)		
181-300	7 (17.5%)	19 (31.67%)		
>301	2 (5%)	4 (6.67%)		
Serum cholinesterase level (IU/l)				
<1000	2 (5%)	4 (6.67%)	*	*
1001-2000	5 (12.5%)	13 (21.67%)		
2001-5000	33 (82.5%)	35 (58.33%)		
>5000	0 (0%)	8 (13.33%)		
*No statistical test was applied- due to 0 subjects in the cells				

Table-3: Comparison of parameters between mechanical ventilation (N=100)

Parameters	Study group		Chi square	P value
	Mortality (N=25)	No Mortality (N=75)		
Age group				
<20	1 (4%)	8 (10.67%)	*	*
21-40	8 (32%)	58 (77.33%)		
41-60	14 (56%)	9 (12%)		
>60	2 (8%)	0 (0%)		
Gender				
Male	23 (92%)	57 (76%)	3.000	0.083
Female	2 (8%)	18 (24%)		
Clinical severity				
I	1 (4%)	16 (21.33%)	61.888	<0.001
II	3 (12%)	55 (73.33%)		
III	21 (84%)	4 (5.33%)		
Time lapse duration in minutes				
<60	6 (24%)	11 (14.67%)	5.866	0.118
61-180	15 (60%)	36 (48%)		
181-300	2 (8%)	24 (32%)		
>301	2 (8%)	4 (5.33%)		
Serum cholinesterase level (IU/l)				
<1000	1 (4%)	5 (6.67%)	*	*
1001-2000	3 (12%)	15 (20%)		
2001-5000	21 (84%)	47 (62.67%)		
>5000	0 (0%)	8 (10.67%)		
*No statistical test was applied- due to 0 subjects in the cells				

Table-4: Comparison of parameters between mortality (N=100)

of serum cholinesterase. Out of 17 participants with grade I clinical severity, 13 (76.47%) participants were serum cholinesterase level 2000 to 5000, 2 (11.76%) participants each had 1000 to 2000 and >5000. Out of 58 participants with grade II clinical severity, 35 (60.34%) participants had serum cholinesterase level of 2000 to 5000, 12 (20.69%) had 1000 to 2000, and 6 (10.34%) participants had level >5000. Out of 25 participants with grade III clinical severity, 20 (80%) participants were serum cholinesterase level 2000 to 5000, and 4 (16%) participants had serum cholinesterase level 1000 to 2000. (Table 2)

Among the 40 participants needing mechanical ventilation, a higher proportion of them was in the older age groups (37.5% in 41 to 60 years and 5% in above 60 years) as compared to people who did not need mechanical ventilation. The proportion of Males was higher among subjects with mechanical ventilation (95% Vs 70%, P value 0.002) Out of 40 participants with mechanical ventilation, majority of 25 (62.5%) participant had grade III clinical severity, and 14 (35%) participant were grade 2 clinical severity—Time-lapsed showed no significant association with mechanical ventilation. Out of 40 participants with mechanical ventilation, majority of 33 (82.5%) participants had serum cholinesterase level was from 2001 to 5000 and 5 (12.5%) participants were serum cholinesterase level 1001 to 2000. (table 3)

Out of 25 people met with mortality, the majority of 14 (56%) participants were aged between 41 to 60 years, and 8 (32%) participants were aged between 21 to 40 years. Out of 25 people met with mortality, 23 (92%) participants were male, and 2 (8%) participants were female. The difference in the proportion of gender between mortality was statistically not significant (p value 0.083). The difference in the proportion of clinical severity between mortality was statistically significant (p value <0.001). The difference in the proportion of time-lapse duration between mortality was statistically not significant (p value 0.118). Out of 25 people met with mortality, the majority of 21 (84%) participants had serum cholinesterase level 20001-,5000 and 3 (12%) participants had serum cholinesterase level 1001-2000. (table 4)

DISCUSSION

Organophosphate poisoning is a serious clinical entity and causes considerable mortality and morbidity. In the present, study OP poisoning predominantly infected males in the age group 21 to 40 years. The majority ha ad moderate poisoning with Serum cholinesterase levels between 2001 to 5000 (IU/l). In this study, the mortality was 25% a, 40% of patients to be ventilated. There was no statistically significant relationship on age, gender, clinical severity, time-lapse, Serum cholinesterase levels, mortality with mechanical ventilation. Mortality rate showed a statistically significant relation with clinical severity (p<0.001).

In the current study according to the POP scale, 17% of patients had a mild grade of poisoning, 58% had a moderate grade of poisoning, 25% patients had severe poisoning with scores more than 8. In a study conducted by Honnakatti et al[10], almost of them belonged to mild grade of poisoning (55%). Similarly, Kh et al[11] reported in a study out of 80 patients, 29 were classified as mild poisoning, 31 as moderate poisoning and 20 as severe as per POP scale.

Serum cholinesterase levels were assessed in all patients at admission to hospital, and it was classified according to Proudfoot. A classification of subclinical (normal), mild, moderate and severe poisoning. Serum cholinesterase levels were < 1000 (IU/l) in 6(6%) participants, 1001 to 2000 (IU/l) in 18(18%), 2001 to 5000 (IU/l) in 68(68%) participants were and>5000 (IU/l) in 8 (8%) participants. Results are in line with Honnakatti et al[10]. reported 48% of patients had >5000 (IU/l) and 7% had < 1000 (IU/l) had serum cholinesterase levels. Both serum cholinesterase and POP scale are an important tool for the diagnosis of the severity of OP poisoning. The higher the POP scale, the higher was the degree of derangement in the serum cholinesterase level. In the present study, increased clinical severity had a statistically significant relationship mortality rate. A study by Goswamy et al[12]. stated that the measurement of serum cholinesterase was useful in predicting the prognosis in OP poisoning. This finding is supported by Chaudhary et al[13] who observed that serum cholinesterase levels between 870 and 1200 on admission were associated with prolonged ventilation and high mortality. However, Aygun et al[5]. have reported that low levels of s. acetylcholinesterase support the diagnosis of acute OP poisoning but was not related to clinical severity. Rehiman et al[14] in 2008 reported that the Peradenya organophosphorus poisoning scale and serum cholinesterase at presentation might be useful to assess the severity of and prolonged duration of hospital stay.

In the current study, the mortality rate was 25%, and 40% were on mechanical ventilation. From previous studies, the estimated mortality from OP ingestion ranges from 10% to 20%.[15] In another study by Sungur et al[17] mortality was 50% in patients requiring mechanical ventilation.[16] In contrast to these observations, Hussain *et al*. reported 8% mortality in patients who received mechanical ventilation. In the present study the overall mortality was 25% which was within the range of the previous studies. A high mortality rate might be due to the greater time taken for admission in the hospital in the present study. Most of the duration from the ingestion of poisoning to initiation of treatment was spent travelling/ arranging transport to the hospital. Efforts to minimize the period between ingestion of poison and initiation of specific treatment may help to decrease the chance of death.

There was no statistically significant relationship on between age, gen time-lapse lapse, Serum cholinesterase levels, mechanical ventilation with death. Only clinical severity had significant relation with mortality. This signifies that death due to OP poisoning is not dependent on a single predictor as age, serum cholinesterase levels and duration of mechanical ventilation etc. Death in OP poisoning is rather due to the overlapping of all these factors.

CONCLUSION

Clinical severity was associated with the treatment

outcomes, including the need for mechanical ventilation and mortality among OP poisoning cases. No particular trend of association was observed between clinical severity and serum cholinesterase levels. Serum cholinesterase levels had shown no association with outcomes. Hence timely administration of antidote dose based on meticulous clinical assessment can minimize the mortality and adverse outcomes among patients with OP poisoning. Such patients need to be monitored closely with good supportive care. Similarly, strict implementation of the pesticide act and involving a new policy by the government to educate the public and youth in large about the dangerous, life-threatening effects of Organophosphorus compounds could help ameliorate the harmful effects of such poisoning.

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