Original Research Article

Study of Association between Serum Cholinesterase Level, Peradeniya Organophosphorus Poisoning Scale and Clinical Outcome in Patients with Acute Organophosphorus Poisoning

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Abstract

Background: Pesticide poisoning accounts for approximately 60% of the estimated 500 000 self-harm deaths in the region each year4. 3 According to many studies, organophosphorus pesticides are responsible for roughly two-thirds of these deaths 5—a total of 200 000 per year. Acute organophosphorus poisoning (AOP) is one of the most common medico toxic emergency in India. Serum cholinesterase levels as a diagnostic marker is well established and but as a prognostic marker, evidenceis lacking. Peradeniya organophosphorus poisoning (POP) scale is easily available scoring systems in predicting the severity with clinical outcome. **Aims and Objectives:**To study the association between serum cholinesterase level, POP scale and clinical outcome in patients with AOP. **Methods:** Thirty-one patients with AOP were studied at Emergency Department of Sri Aurobindo Medical College and PG Institute, Indore, from December 2017 to May 2019. Estimation of serum cholinesterase levels and categorization based on POP scaleas Mild (0-3), Moderate (4-7) and Severe (8-12) was done and compared with hospital stay, ventilatory support, and mortality. **Results:** AOP was more prevalent in males (74.2 %). Serum cholinesterase levels of patients had no significant association with total duration of hospitalization ($p>0.05$) but was significant factor that influenced the clinical outcome (death). POP scale grading of patient with AOP was the significant factor that strongly influence the total duration of hospitalization ($p<0.003$), duration of ventilator support ($p<0.001$) and clinical outcome ($p<0.001$). **Conclusion:** POP scale is a better prognostic marker due to significant association between POP scale and clinical outcome, requirement, and duration of ventilatory support and total duration of hospitalization.

Keywords: Prognostic marker, poisoning, serum cholinesterase, toxicity, organophosphorus compound

Introduction

As per the World Health Organization (WHO) pesticide toxicity has become one of the important global problem affecting more than 2 lakhs of death every year. Majority of the poisoning cases are from the Southeast Asia. India being the hub of farming, use of pesticide containing organophosphorus compound is frequent for crop protection and pest control. Hence, it exerts many detrimental effects on the health of people[1].Mortality due to organophosphorus compound poisoning is as high as 70 %. Lack of hospital services in the remote area, insufficient transport facility, delay in initiation of suitable treatment and non- availability of definite antidote are the reason for this high mortality[2].Assessment by clinical markers isimportant step to classify severity of poisoning and early referral to higher centre where aggressive treatment can be initiated immediately to control the spread of poisoning. Several studies have been performed to assess the diagnostic and prognostic value of serum cholinesterase levels in organophosphorus compound poisoning and association with the poisoning symptoms[3,4]. Majority of the studies have reported the usefulness of serum cholinesterase as the diagnostic marker but as a prognostic marker its role is limited[5,6]. Hence, it is necessary to compare the easily available scoring systems in predicting the severity with clinical outcome. In present study we tried to determine the association between serum cholinesterase level, POP scale and clinical outcome in patients with acute organophosphorus poisoning.

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Methods

A cross sectional study was conducted at Sri Aurobindo Medical College and PG Institute, Indore, over a period of 18 months from December 2017 to May 2019 on 31 patients with AOP who presented to Hospital Emergency Department. The informed consent was obtained from patient's attenders.Purposive sampling (Non-probability sampling) technique was employed to recruit the desired samples from the population of patients with AOP.All cases with alleged history of consumption/ inhalational or exposure of organophosphorus compounds and those with presence of characteristic clinical signs and symptoms of organophosphorus compound poisoning were included. Patients/ attenders not willing for the study, cases with history of consumption/inhalation or exposure of an entirely different poison other than organophosphorus poison and patients who did not complete medical management were excluded. The patient/ attenders were explained about the complete treatment procedure, and complete information about study, its benefits, and its future prospects, in his/her own language and his/her willingness to undergo for the same was recorded in a consent form duly signed by him.All the patients were thoroughly investigated. All the relevant medical, personal, and surgical history was obtained. The diagnosis of AOP was made on following criteria: history of consumption/ inhalation/ exposure with pesticide containing organophosphorus compounds; characteristic clinical signs and symptoms of organophosphorus poisoning and improvement of signs and symptoms after treatment with atropine and oximes (Pralidoximes).All patients were subjected to serum cholinesterase levels estimation and categorization based on Peradeniya organophosphorus poisoning scale as Mild (0-3), Moderate (4-7) and Severe (8-12) and compared with hospital stay, ventilatory support, and mortality.

Responses of frequencies were calculated and analysed by using the raw data of 31 subjects. The raw data were entered into the computer database. Statistical software, SPSS version 17.0. Trial was used for analysis. Prevalence of an outcome variable along with 95 % confidence limits was calculated. Both, descriptive and inferential statistics were used to study clinical profile and the clinical outcomes in patients with AOP. Descriptive statistics were used to depict the main features and characteristic of the collected samples of Acute Organophosphorus poisoning. Results on continuous measurements are presented on Mean ± Standard Deviation (Min-Max) and results on categorical measurements are presented in numbers (%).

Results

Out of 31 patients with AOP, majority were males accounting for approximately three-fourth (74.2 %) of the population. Mean age of study cohort was 38.42±16.31 years which ranged from 15 to 80 years. Mean time of presentation after poisoning to hospital was 73.23±56.96 minutes which ranged from 15 to 300 minutes.

Relationship of serum cholinesterase levels and Peradeniya Organophosphorus poisoning (POP) scale gradings of patients with Organophosphorus poisoning was identified with total duration of hospitalization, ventilatory support and clinical outcome.

Table 1: Association of Total Duration of Hospitalization of Patient with Serum Cholinesterase Level

Serum Cholinesterase Level (kilo unit per Liter)	Duration of Hospitalization (days)			Total	P Value
	0-7	7-14	≥14		
<1.00	7 (22.6)	3 (9.7)	2 (6.5)	12 (38.7)	>0.05
1.00-4.62	5 (16.1)	4 (12.9)	0 (0.0)	9 (29.0)	
≥4.62	9 (29.0)	1 (3.2)	0 (0.0)	10 (32.3)	
Total	21 (67.7)	8 (25.8)	2 (6.5)	31 (100.0)	

Serum cholinesterase levels of patients did not have significant impact on total duration of hospitalization (p>0.05). Henceforth, the Serum cholinesterase levels of patients with acute Organophosphorus poisoning was found to be independent factor of total duration of hospitalization.

Serum cholinesterase level of most (25.8 %) of the patients was found to be less than 1.00 kilounit per liter who needed ventilator support for 1 to 7 days as compared to 5 (16.1 %) who had serum cholinesterase level between 1.00 to 4.62 kilounit per liter.The proportional differences indicated that the duration of ventilator support of 2 (6.5 %) patients was found to be between 7 and 13 days and had serum cholinesterase level of less than 1.00 kilounit per liter. Further, results showed that the level of serum cholinesterase of only 1 (3.2 %) patient was found to be less than 1.00 kilounit per liter and had duration of ventilator support of more than 13 days.The serum cholinesterase level of 10 (32.3 %) patients who did not require ventilator support was more than or equal to 4.62 kilo unit per liter. Hence, the association of duration of ventilator support of patients with serum cholinesterase levels was found to be statistically highly significant (p<0.002). This indicated that the serum cholinesterase level of patient with acute organophosphorus poisoning was the significant factor that influenced the duration of ventilator support.

Table 2.:Association of Clinical Outcome of Patient with Acute Organophosphorus Poisoning with Serum Cholinesterase Level

Serum Cholinesterase Level (kilo unit per liter)	No of Patients withOrganophosphorus Poisoning		Total	P Value
<1.00	5 (16.1)	7 (22.6)	12 (38.7)	0.004
1.00-4.62	8 (25.8)	1 (3.2)	9 (29.0)	
≥4.62	10 (32.3)	0 (0)	10 (32.3)	
Total	23 (74.2)	8 (25.8)	31 (100.0)	

Serum cholinesterase level of majority (10, 32.3 %) of patient was found more than or equal to 4.62 kilounit per liter were discharged as compared to 8 (25.8 %) and 5 (16.1 %) patients who had serum cholinesterase level between 1.00 to 4.62 kilounit per liter and < 1.00 kilounit per liter respectively and were discharged.Further, results showed that the level of serum cholinesterase of 7 (22.6 %) patientswas found to be less than 1.00 kilounit perlitre in whom the clinical outcome was death. However, the clinical outcome in 1 (3.2 %) case was death who had serum cholinesterase level between 1.00 to 4.62 kilounit per liter.Serum cholinesterase level of patient with AOP found to be the significant factor that strongly influenced the clinical outcome.Grading of POP scale of 15 (48.4 %) patient was found to be more frequently mild and had duration of hospitalization between 0 to 7 days as compared to 1 (3.2 %) and 5 (16.1 %)who had moderate and severe grading of severity respectively rated on POP scale.Henceforth, the statistical agreement indicated that the POP scale grading of patient with AOP was the significant factor that strongly influence the total duration of hospitalization (p<0.003).

Table 3:Association of Duration of Ventilator Support of Patient with Acute OrganophosphorusPoisoning with POP Scale Grading

POP Scale Score (Grading)	Duration of Ventilator Support				Total	P Value
	No Support	1-7 days	7-13 days	≥13 days		
0-3 (Mild)	15 (48.4)	2 (6.5)	0 (0)	0 (0)	17 (54.8)	<0.001
4-7 (Moderate)	0 (0)	6 (19.4)	1 (3.2)	1 (3.2)	8 (25.8)	
8-12 (Severe)	0 (0)	5 (16.1)	1 (3.2)	0 (0)	6 (19.4)	
Total	15 (48.4)	21(67.7)	8 (25.8)	2 (6.5)	31 (100.0)	

It was found that 51.6 % patients with acute organophosphorus poisoning required ventilator support but rest 48.4 % patients did not required ventilator support. Severity on POP scale among majority of (19.4 %) patients was found to be more frequently moderate and had duration of ventilator support between 1 to 7 days. However, duration of ventilator support of 5 (16.1 %) and 2(6.5 %) patients was between 1 to 7 days and had severe and mild grading of severity respectively according to POP scale gradings.Results showed that the degree of severity according to POP scale of only one (3.2 %) patient was found to be moderate and had duration of ventilator support of more than or equal 13 days.This was also noted that the POP scale level of fifteen (48.4 %) patients who did not require ventilator support found to be mild. Henceforth, the statistical agreement indicated that the POP scale grading of patient with acute Organophosphorus poisoning was a significant factor that influenced the duration of ventilator support (p<0.001).Severity on POP scale of 17 (54.8 %) patients was found to be mild who were discharged as compared to 6(19.4 %) patients who had moderate degree of severity on POP scale grading were also discharged. Level of POP scale of 6 (19.4 %) patient was found to be severe in whom the clinical outcome was death. However, the clinical outcome in 2 (6.5 %) cases was death who had moderate degree of severity. Henceforth, the statistical agreement indicated that The POP scale grading of patients with acute organophosphorus poisoning was found to be a significant factor that strongly influenced the clinical outcome (p<0.001).

Discussion

Organophosphate compounds are widely used as insecticide in agriculture. Because they are easily available, accessible, and used widely, organophosphate toxicity is a significant universal health concern mainly in unindustrialized countries. One of the supreme causes of suicidal deaths in India is Organophosphate ingestion. Serum cholinesterase level and POP scale are frequently used for the

diagnosis of level of poisoning[7]. In present study we tried to evaluate the association between serum cholinesterase level, POP scale and clinical outcome in patients with acute organophosphorus poisoning.In our study we found highly significant association ($p<0.001$) between POP scale and ventilatory support. Out of 31 patients 17 patients(54.9 %)were in mild grade of POP scale, 15 patients(89 %) of these 17 did not required ventilatory support and only 2 patients(11 %) required ventilatory support. Out of 31 patients all 8 patients (25.8 %) of moderate grade required ventilatory support, all 6 patients (100 %) of severe grade required ventilatory support.

This is in accordance with study findings of Chaudhary et alin which all 22 patients(100 %) of severe grading required ventilatory support, 49 patients(63.4 %) out of 75 in moderate grade required ventilatory support and all 53 patients of mild grade did not required ventilatory support and hence indicates that higher the POP score, higher will be the chances ventilatory support requirement[7]. Study done by Patel et alshowed 47 patients(47 %) in mild grade did not required ventilatory support, 4 patients out of 41(9.7 %) in moderate grade required ventilatory support and all 12 patients(100 %) in severe grade required ventilatory support and hence had statistically significant association($p<0.01$)[8].In our study we also found the association of POP scale and final clinical outcome of the patients which were highly significant ($p<0.001$). Out of 31 patients, 17 (54.8 %) were in mild grade and all of them survived and were discharged. Out of total 31 patients 8 (25.8 %) were in moderate grade and 6 of these (75 %) survived and 2 patients(25 %) died and all 6 patients(19.4 %) out of 31 in severe grade died. It is similar to study done by Chaudhary et al in which all 53 patients(35.33 %) in mild grade survived, 30 out of 75 patients(40 %) of moderate grade died and 45 patients(60 %) survived and out of 22 patients(14.67 %) of severe grade 19 patients died and 3 survived and were discharged, hence they also found association statistically significant($p=0.034$) between POP scale and clinical outcome[7].Present study also found a highly significant association between serum cholinesterase levels and ventitalory support and highly significant association ($p<0.004$) between serum cholinesterase level and clinical outcome. It was noted that out of 12 patients(38.7 %) of total 31 patients who had severe poisoning (<1.00 KU/L) 11 patients required ventilatory support(92 %) and 7 died(59 %) while 5 (41 %) survived out of these 12 patients. In our study there was no significant association between the serum cholinesterase level and duration of hospital stay.Out of 9 patients in moderate poisoning (1.00-4.62 KU/L) only 5 patients(56 %) required ventilatory support and only 1 (11 %) died and rest 8(91 %) survived out of these 9 patients. Rest 10 patients (32.3 %) out of total 31 who were having mild poisoning(>4.62 KU/L) did not required ventilatory support and all of them survived and were discharged. It is in accordance with study done by Chaudhary et alwhich showed that all 23 patients (15.33 %) having severe poisoning(<10 %cholinesterase level) required ventilatory support and 20 patients (87 %) out of these 23 died while 3 (13 %) of them survived. 77 patients were having moderate poisoning(20-50 % of level) out of which 48(64 %) required ventilatory support and out of those 77 patients, 29(38.7 %)died while 48 (61.3 %) survived. 45 patients were having mild poisoning(>50 % of level), all of them survived and none of them required ventilatory support[7]. Study done by Kang et al found decreased serum cholinesterase level in all 13 patients who died out of 68 patients they studied. Hence, they found a direct correlation between decreased serum cholinesterase level and mortality which was statistically significant and similar to findings of our study[9]. However study done by Twayana RS et al found that there was a significant correlation between the lower serum cholinesterase level and duration of hospitalization but there was no significant correlation between lower serum cholinesterase level and need for ventilatory support[10].

At last, in our study, we found that out of 31 patients, 23 patients(74.2 %) survived and were discharged, and 8 patients (25.8 %) died which is slightly higher than the studies compared in literature. Kumar et al[11] had 17.5 %mortality, Agrawal et al[12] had 22 %mortality rate, Rajeev H. et al[13] had only 8 %mortality rate and Patel et al[8]had 9 % mortality rate. However,mortality rate of one study done by Chaudhary et al was 32.7 %. [7]Study done by Kang et almortality rate was 19 % in their study(13/68 patients).[9]Study done by Laudari et al mortality rate was 7.69 %[14].The higher mortality rate in our study can be attributed to the fact that out of 8 mortality, 7 patients had serum cholinesterase level <1.00KU/L which signifies severe poisoning and 1 patient had moderate poisoning i.e.,serum cholinesterase level between 1.00-4.62 KU/L.And as discussed above in different studies serum cholinesterase level is inversely proportional to mortality, less is serum cholinesterase level more is mortality. Also, on POP scale out of 8 mortality, 6 of them were in severe grading of POP scale and 2 in moderate grading of POP scale, which further explains the mortality of 8 patients as it is established by other studies discussed above that severe and moderate degree of POP scale has more mortality rates.Another factor which can explain the high mortality rates is time of reaching the hospital after poisoning. Majority of these 8 patients presented late to hospital mainly after 2 hours as they took primary treatment outside in a primary health care centre and thus presented late to our centre, along with that they also consumed more than 100 ml of poison due to which these patients could not survive and hence these are the other significant contributing factors for the Mortality of these 8 patients. One more factor which can explain higher mortality rate is our hospital being tertiary care centre due to which many patients present first present in primary health centre and then come to our centre for treatment thereby causing a delay in specific treatment of these patients. However, since the sample size of our study was small (31 patients), a large sample size study is required to ascertain the definitive and precise mortality rate and usefulness of significant prognostic markers for AOP.

Conclusion

We found that POP scale is a better prognostic marker as our results has showed highly significant association between POP scale and clinical outcome, requirement, and duration of ventilatory support and total duration of hospitalization. Serum cholinesterase levels is also found to be a good prognostic marker as our results showed highly significant association between serum cholinesterase level and clinical outcome and requirement and duration of ventilatory support. However, there was no significant association between serum cholinesterase level and total hospitalization. Hence, it is proved that POP scale is a better prognostic marker as compared to serum cholinesterase levels.

Hence, POP is a better clinical tool in assessing the further outcome of the patient and should be invariably performed in all the patients of AOP.

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