Original Research Article

A study to correlate serum pseudocholinesterase and serum creatine phosphokinase levels in acute organophosphorus poisoning with respect to Peradeniya organophosphorus poisoning scale

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ABSTRACT

Background: Organophosphorus insecticides are one of the most common causes of poisoning in India. It has a high mortality rate and accounts for a third of suicidal deaths in south-east Asia.

Methods: The objectives were to estimate serum pseudocholinesterase and creatine phosphokinase (CPK) levels in organophosphorus poisoning and correlate them with the severity and prognosis described by the Peradeniya organophosphorus poisoning (POP) scale at initial presentation. This was a cross-sectional study conducted over 18 months. A total of 180 organophosphorus-poisoning subjects were divided into mild, moderate and severe grades based on POP scale at admission. Serum pseudocholinesterase and CPK levels were estimated at admission. The outcome was noted, and the results were statistically analysed.

Results: It was found that 112 (62.2%), 51 (28.3%) and 17 (9.4%) patients had mild, moderate and severe poisoning, respectively, according to POP scale. Mean pseudocholinesterase level (units/litre) was 2393.29, 1104.37 and 638.18 and mean serum CPK level (units/ litre) was 153.41, 344.94 and 280.53 in mild, moderate and severe poisoning, respectively. ICU and ventilator were required for 84 (46.75%) and 72 (40%) patients, respectively. Mortality was 17.8%. Negative, weak and significant correlation was seen between POP score and pseudocholinesterase (r=-0.265, p=0.00). Positive, moderate and significant correlation was seen between POP score and CPK levels (r=0.449, p=0.00).

Conclusions: POP scale applied at admission along with serum pseudocholinesterase and CPK levels serve as a simple and effective system to determine early need for ventilation and mortality in rural, peripheral centres in developing nations.

Keywords: Organophosphorus, Pseudocholinesterase, CPK, POP scale

INTRODUCTION

Organophosphorus (OP) compounds are a major contributor to poison-associated morbidity and mortality in India. The world health oirganization (WHO) estimates that globally 3 million intentional or unintentional pesticide poisoning episodes occur annually and out of these, a minimum of 300,000 die.[1] The incidence is higher in adolescents and young people, in developing countries, with mortality rates ranging from 10 to 20%.[2] Occupational exposure to organophosphorus compound accounts for about 20% of patients, with mortality being about 1%. Accidental poisoning and homicidal use account for 8-10% and <1% of the incidents, respectively.[3]

Various prognostic tools such as serum CPK, lactate dehydrogenase (LDH), serum immunoglobulins, and circulating complements for early detection of patients at high risk for developing respiratory failure have been tried.[4] Thereis an elevation of serum CPK in OP poisoning due to myonecrosis and oxidative cellular damage to the muscle membrane.[5-6] Serum CPK level has also been studied as a predictor for the onsetof IMS.[7] POP scale is a well-known tool used to classify the severity of poisoning.[8]

With this scenario, the present study was designed to establish a prognostic correlation with levels of serum pseudocholinesterase and serum CPK in OP poisoning. The levels of the two were used to assess the severity of OP poisoning and to correlate with the clinical criteria described by the POP scale at initial presentation and the severity of poisoning for use as prognostic biomarkers of OP poisoning.

The aims and objectives of the study are to estimate serum pseudocholinesterase and serum CPK levels in OP poisoning and to correlate with the clinical criteria described by the POP scale at initialpresentation and the severity of poisoning.

METHODS

Methodology

The study was conducted on patients presenting to hospitals attached to Bangalore medical college and research institute from November 2018 to May 2020. The study design was an observational cross-sectional study including 180 subjects who were more than 18 years of age. After obtaining approval and clearance from the institutional ethics committee, the patients fulfilling the inclusion criteria were enrolled for the study after obtaining informed consent. Data was collected using a preformed proforma from each patient. Study groups were formed. Data was collected based on clinical examination, patient case sheets andinvestigations. On admission, levels of serum CPK and serum pseudocholinesterase levels were measured, and assessment was also done based on POP scoring system. Need for ventilator support, mortality was noted, and results were statically analysed using p value.

Inclusion criteria

All the patients above 18 years of age willing to give informed consent with an alleged history of OP poisoning (ingestion/inhalation/contamination) and diagnosed to have consumed OP poison within 24 hours of presentation were included.

Exclusion criteria

Patients less than 18 years of age with H/o consumption of OP compound with other poison/drugs; other comorbid conditions like pneumonia, COPD, malignancy, chronic liver disease, neuromuscular diseases like myasthenia gravis or muscular dystrophy; patients who did not give informed consent were excluded.

Assessment tools

Patients were assessed using complete blood count,random blood sugar, renal function test, liver function test, POP scale, serum pseudocholinesterase levels and sSerum CPK levels.

POP scale is a scoring system introduced by Senanayake et al in 1993 wherein five common clinical manifestations of OP poisoning viz. miosis, fasciculation, respiration, bradycardia, and level of consciousness have been selected as parameters. Each parameter was to be assessed on a 3-point scale varying from 0-2. Poisoning can then be graded as mild (score 0-3), moderate (score 4-7) or severe (score 8-11) when the patient first presents (Table1).[8]

Table 1: Description of POP scale.

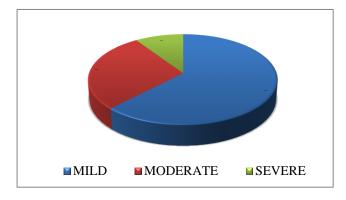| Parameters	Score
Miosis	
Pupil size >2 mm	0
Pupil size ≤2 mm	1
Pupils pin-point	2
Fasciculation	
None	0
Present but not generalised or continuous	1
Generalised or continuous	2
Respiration	
Respiratory rate ≤20/min	0
Respiratory rate >20/min	1
Respiratory rate >20/min with central cyanosis	2
Bradycardia	
Pulse rate >60/min	0
Pulse rate 41-60/min	1
Pulse rate ≤40/min	2
Level of consciousness	
Conscious and rational	0
Impaired, responds to verbal commands	1
Impaired, no response to verbal commands	2
If convulsions present, add	1
Total	11

Statistical analysis

Based on POP scale, patients were categorised into mild, moderate and severe. The data collected were analysed statistically using descriptive statistics, namely mean, standard deviation, percentage wherever applicable. Appropriate parametric and non-parametric tests were used. Pearson's partial correlation coefficient between POP scale, serum CPK level and serum pseudocholinesterase level were analysed.
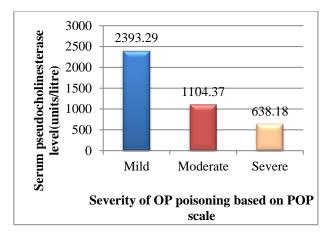
RESULTS

Out of a total of 180 patients, the mean age of the patients was 35.01±13.708 years with a minimum age of 18 years and maximum age of 82 years. A maximum number of patients, i.e., 130 (72.2%) patients, were males, whereas females were 50 (27.8%). Out of total,60 (33.3%) patients were aged between 26 to 35 years followed by 51 (28.3%) patients aged less than 25 years, 31 (17.2%) patients aged between 36 to 45 years, 21 (11.7%) patients aged between 46 to 55 years and 17 (9.4%) patients aged above 55 years.

The OP poisoned patients were distributed based on POP scale mild, moderate and severe. It is seen that a majority of patients (62.2%) had mild poisoning in Figure 1.
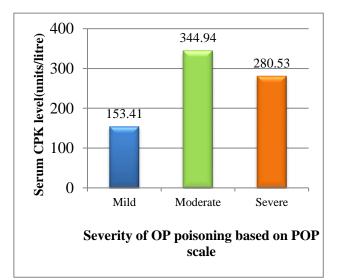

Figure 1: Distribution of patients based on POP scale.

Out of 84 patients who required ICU, 46 (90.2%) were in the moderate POP category. Similarly, out of 72 patients who required ventilator, 39 (76.5%) were in the moderate POP category. Mortality was high in patients having a severe POP score. Chi-square was applied to associate the POP category with ICU requirement, ventilator requirement and mortality. Chi-square test showed statistically significant association between POP category and ICU requirement (p=0.00), ventilator requirement (p=0.00) and mortality (p=0.00) (Table 2).

Figure 2: Comparison of *S. pseudocholinesterase* level (units/litre) amongthe POP scale groups using Kruskal-Walli's test.

Figure 3: Comparison of serum CPK levels (units/litre) among the groupsclassified by POP scale using Kruskal-Wallis test.

Table 2: POP scale with ICU requirement, ventilator requirementand mortality rate.

Variables			POP scale				Chi-square value	P value
			Mild	Moderate	Severe	Total		
ICU requirement	No	Count	91	5	0	96	93.32	0.00*
		%	81.2	9.8	0.0	53.3		
	Yes	Count	21	46	17	84		
		%	18.8	90.2	100	46.7		
Ventilator requirement	No	Count	96	12	0	108	84.62	0.00*
		%	85.7	23.5	0	60		
	Yes	Count	16	39	17	72		
		%	14.3	76.5	100	40		
Mortality	No	Count	110	38	0	148	100.29	0.00*
		%	98.2	74.5	0	82.2		
	Yes	Count	2	13	17	32		
		%	1.8	25.5	100	17.8		

*Significant.

Table 3: *S. pseudocholinesterase* levelswith ICU requirement, ventilator requirement and mortality.

Variables			S. pseudocholinesterase					Chi-square value	P value
			Mild	Moderate	Severe	Normal	Total		
ICU requirement	No	Count	9	13	60	14	96	14.1	0.003*
		%	90	65	45.5	77.8	53.3		
	Yes	Count	1	7	72	4	84		
		%	10	35	54.5	22.2	46.7		
Ventilator requirement	No	Count	9	16	69	14	108	12.73	0.005*
		%	90	80	52.3	77.8	60		
	Yes	Count	1	4	63	4	72		
		%	10	20	47.7	22.2	40		
Mortality	No	Count	10	18	102	18	148	9.09	0.028*
		%	100	90	77.3	100	82.2		
	Yes	Count	0	2	30	0	32		
		%	0.0	10	22.7	0	17.8		
Total		Count	10	20	132	18	180		
		%	100	100	100	100	100		

*Significant.

Table 4: S. CPK levels with ICU requirement, ventilator requirement and mortality.

Variables			S. CPK				Chi-square value	P value
			High	Low	Normal	Total		
ICU requirement	No	Count	12	1	83	96	30.45	0.00*
		%	22.2	100	66.4	53.3		
	Yes	Count	42	0	42	84		
		%	77.8	0.0	33.6	46.7		
Ventilator requirement	No	Count	14	1	93	108	37.59	0.00*
		%	25.9	100	74.4	60		
	Yes	Count	40	0	32	72		
		%	74.1	0	25.6	40		
Mortality	No	Count	32	1	115	148	27.87	0.00*
		%	59.3	100	92	82.2		
	Yes	Count	22	0	10	32		
		%	40.7	0	8	17.8		
Total		Count	54	1	125	180		
		%	100	100	100	100		

*Significant.

Out of 84 patients who required ICU, 72 (54.5%) had severe serum pseudocholinesterase levels. Similarly, out of 72 patients who required ventilator, 63 (47.7%) had severe serum pseudocholinesterase. Mortality was high in patients having severe serum pseudocholinesterase levels, i.e., 30 (22.7%). Chi-square test was applied to associate the Serum pseudocholinesterase levels with ICU requirement, ventilator requirement and mortality. Chi-square test showed a statistically significant association between Serum pseudocholinesterase levels and ICU requirement (p=0.003), ventilator requirement (p=0.005) and mortality (p=0.028) (Table 3).

Of patients who required ICU, out of 84 patients, 42 (77.8%) patients had high serum CPK levels. Similarly, out of 72 patients who required ventilator, 40 (74.1%) had high serum CPK levels. Mortality was high in patients

having severe serum CPK scores-22 (40.7%). A chi-square test was applied to associate the serumCPK levels with ICU requirements, ventilator requirement and mortality. Chi-square test showed a statistically significant association between serum CPK levels and ICU requirement (p=0.00), ventilator requirement (p=0.00) and mortality (p=0.00) (Table 4).

Table 5: Spearman's correlation between POP score and *S. pseudocholinesterase*, POP score and s. CPK.

Correlation	R value	P value
POP score vs s. pseudocholinesterase	-0.265	0.00*
POP score vs s. CPK	0.449	0.00*

*Significant.

Spearman's correlation was applied to correlate POP score with serum pseudocholinesterase and serum CPK levels. A weak, negative and significant correlation was seen between POP score and Serum pseudocholinesterase (r=-0.265, p=0.00). A positive, moderate and significant correlation was seen between POP score and S.CPK levels (r=0.449, p=0.00) (Table 5).

DISCUSSION

Organophosphorus compound poisoning is a common health problem in third world countries. The major cause of morbidity and mortality in OP poisoning is respiratory failure, and patients may require ventilator support & ICU care. But in developing nations like India, where ICU facilities may not be readily available because of limited resources and patient load, stratification of patients carrying a high risk of developing respiratory failure and intense monitoring of those patients play a crucial role in reducing mortality.

The CPK activity was significantly elevated in poisoning cases and more significant changes in the patients who died due to poisoning. In our study, a similar result in elevation of serum CPK levels has been observed. Mean serum CPK levels in those patients with mild grading of poisoning were 153.41 units/litre; in moderate grade poisoning, the mean value was 344.94 units/litre, and in severe poisoning, the mean elevated to 280.53 units/litre, respectively. When the associations of serum CPK among the groups classified by POP scale were submitted to statistical analysis by Kruskal-Wallis test, it was found to be statistically significant with p=0.00. These observations were comparable to the studies done by Subhash et al and Kavya et al.[9,10]

The mean pseudocholinesterase levels in those patients with mild grading of poisoning were 2393.29 units/litre; in moderate grade poisoning, the mean value was 1104.37 units/litre. In severe poisoning, the mean value dropped down to 638.18 units/litre, which was found to be statistically significant with p=0.00. These observations were comparable to the studies done by Subhash et al. and Kavya et al.[9,10]

If a clinical sign or a symptom or a lab value is useful in predicting deterioration in OP poisoning, it will be easy for the clinicians to stratify the patients according to the risk of developing respiratory failure and arrange ventilator support for them. Hence the number of patients requiring ICU, ventilator and mortality rate was noted. ICU was required for 84 (46.7%) patients, the ventilator was required for 72 (40%) patients. Mortality was observed in 32 (17.8%) out of 180 (100%) patients. In a study done by Kavya et al., the percentage of patients requiring ventilator support was found to be 80%.[10] Only 14.3% of patients with a mild grade of poisoning needed ventilator support, while 100% of patients with severe poisoning required ventilator assistance. This relation was statistically significant. These observations were comparable to the studies done by Subhash et al and Kavya et al.[9,10] Among OP poisoning patients, 2 (10%) patients with moderate and 30 (22.7%) patients with severe reduction serum pseudocholinesterase have died and were statistically significant. Similarly, 22 (40.7%) patients with high serum CPK levels died, which was found to be statically significant. The association of serum CPK and requirement of ICU and ventilator was found to be statistically significant.

It was found that a weak negative Spearman's correlation was seen with serum pseudocholinesterase and POP score, which was statistically significant, whereas Spearman's correlation showed a positive moderate and significant correlation between POP score and serum CPK levels.

CONCLUSION

The POP scale applied at admission is an easy, quick and inexpensive method in predicting the outcome in terms of morbidity and mortality. The rising trend of serum CPK and a falling trend of serum pseudocholinesterase indicates severe poisoning, so both can be used as severity markers and prognostication markers to anticipate complications. The results based on this study suggests some level of correlation between the POP score, which is based on clinical features, and the biochemically measured serum pseudocholinesterase and serum CPK levels on admission. It could be a simple and effective system to determine early the need for ventilation and mortality in rural and peripheral centres in developing nations.

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