

Study of POP score, serum cholinesterase and serum creatine phosphokinase in organo phosphorus poisoning

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Abstract

Background: Organophorous compounds are commonly used for suicide in developing country like India due to their easy availability. This study was undertaken to correlate Peradeniya organophosphorus scoring, serum CPK level and Plasma cholinesterase level at time of admission with ventilator requirement and mortality. **Material and Methods:** This was a retrospective study done at Government Medical College and S.S.G Civil hospital Vadodara , Gujarat. Over a period of two year 150 patients fulfilling inclusion criteria, were included and patients were categorized according to Peradeniya organophosphorus poisoning (POP) scale. Level of serum CPK, and plasma cholinesterase were measured on admission. Their relation in respect to ventilator requirement and mortality were assessed statistically using Chi Square test. **Results:** In study of 150 patients, maximum incidence is in 20-29 years of age group (34%). Males (77%) are more affected as compared to females (23%). Maximum cases were related to suicidal intent (86 %) followed by accidental exposure (14%). According to POP scale 24% cases had mild poisoning and 69% cases had moderate while 07% patient were severely poisoned. Correlation of POP score, Plasma Cholinesterase (PCh) level and serum CPK level with ventilator support requirements and mortality was determined statically. Significant (p value <0.0001) correlation found between them except for PChE and ventilator support (p value <0.08). **Conclusion:** We recommends routine use of POP score at primary health care settings to classify OP patients according to their severity and timely refer them to higher center to reduce mortality. We also recommend S. CPK level to be used as routine biomarker of severity in OP patients along with PChE level to study its efficacy as a prognostic marker.

Key Word: Peradeniya organophosphorus poisoning (POP) scale, Plasma Cholinesterase, Serum Creatine Phosphokinase, Ventilator Requirement

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INTRODUCTION

Organophosphorus (OP) compound poisoning is an important global health issue especially in developing countries like India because of their widespread use and

easy accessibility^{1,2}. In many Indian reports, the rates of poisoning as suicidal method ranges from 20.6% (10.3% organophosphorus) to 56.3% (43.8% organophosphorus)^{3,4}. The commonly encountered OP compounds comprise insecticides (including malathion, parathion, diazinon, fenthion, dichlorvos, chlorpyrifos, ethion), nerve gases (including soman, sarin, tabun, VX), ophthalmic agents (echothiophate, isofluorophate), antihelmintics (such as trichlorfon) and herbicides [including tribufos (DEF), merphos which are tricresyl phosphate containing industrial chemicals]. They act by inhibiting the acetylcholinesterase enzyme (AChE) at muscarinic and nicotinic receptors, producing an array of clinical manifestations like miosis, bradycardia, increased gastrointestinal motility, emesis, sweating, tachypnea, salivation, lacrimation, altered sensorium, fasciculation,

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bronchospasm, blurred vision, photophobia, urination and defecation. Till now, investigations comprised erythrocyte cholinesterase (EchE) and plasma cholinesterase (PchE) estimation, the levels of which are reduced in OP poisoning. But estimation of their levels is costly and not regularly performed in most laboratories of our country. Besides this, the kinetic study of inhibition of human AchEs by Demeton-S-methyl has shown that cholinesterase-based titration methods are not suitable for the estimation of OPs.⁵ Several animal model studies on rat liver and fresh-water snails indicate the association between OP poisoning and CPK levels.⁶ In an earlier study, it was proposed that serum level of CPK is often found to be elevated in OP poisoning and may be used as a biomarker⁷. Considering this background we planned a study to assess the correlation of POP score, PChE level and serum CPK level with the severity of acute OP poisoning that measured by ventilator support and mortality. We tried to understand the clinical and prognostic significance of CPK in OP poisoning and to assess if serum CPK level can be used as an alternative of plasma ChE level to stratify OP poisoning severity.

MATERIALS AND METHODS

After obtaining Institutional Ethical Committee approval and written informed consent from patients or their caregiver, this observational type of study was conducted in 150 patients who were admitted in the department of medicine in our tertiary care hospital (S.S.G Hospital - Vadodara) for a period of 2 year (2015 & 2016) of either sex, having age >12 years, presented within 12 hour of ingestion or inhalation. The cases with chances of exposure to an entirely different poison other than OP poison, patients with OP poisoning which was mixed with

any other poison, chronic alcoholics patients, patients who had history of chronic liver disease, myopathy, history of malignancy, renal disease and history of intake of drugs like –statins, fibrates, dexamethasone, aspirin, anticoagulants, frusemide were excluded from study. Confirmation of OP poisoning was done by seeing the packet/container with clinical presentation.

After initial resuscitation and stabilization of patients, blood samples were collected aseptically by a single prick, from a peripheral vein without tying any tourniquet. The levels of serum CPK and serum cholinesterase were measured following admission. CPK levels were estimated spectrophotometrically using the commercial kit of creatinkinase and by using UV kinetic optimized method. A preformed and pre-tested proforma was used to collect information from patients detailed history, clinical examination and relevant biochemical investigations were done. Patients were evaluated at time of admission and were followed up during treatment till their final clinical outcome and whether they required ventilator support or not was noted.

Based on the assessment as described in below table, a score was given to the patients. A score of 0 to 3 is considered as mild poisoning, 4 to 7 as moderate poisoning and 8 to 11 as severe poisoning. Data after collection were tabulated in Microsoft excel and later Online software Social Science Statistics was used for analysis of data. Pearson's Chi square test was used to analyse data. By using the above mentioned tests, level of significance was calculated. A 'p' value less than 0.05 is statistically significant. Clinical severity was categorized according to Peradeniya organophosphorus poisoning (POP) scale as shown in below Table.

Peradeniya Organophosphorus Poisoning (POP) Scale ⁸		
Pupil size	>2mm	0
	<2mm	1
Respiratory rate	Pin point	2
	<20/min	0
	>20/min	1
	>20/min with central cyanosis	2
Heart rate	>60/min	0
	41 to 60/min	1
	<40/min	2
Fasciculations	None	0
	Present, generalized or continuous	1
	Both generalized and continuous	2
Level of consciousness	Conscious and rationale	0
	Impaired response to verbal commands	1
	No response to verbal commands	2
Seizures	Absent	0
	Present	1

RESULTS

Total 150 patients were enrolled in the study. Of them, maximum incidence is in 20-29 years of age group (34%). while Incidence in 30-39 years age is 23%, 13-19 years and >50 years age group show 15 % incidence. The present study shows more incidence in males (77%) compared to females 23%). Maximum cases were related to suicidal intent (86 %) followed by accidental exposure/ingestion(14%). The present study shows maximum cases presented within 6 hours of poisoning (64%). According to POP scale 24% cases had mild poisoning and 69% cases had moderate while 07% patient were severely poisoned (Table 1). 07 out of 12 patients who were severely poisoned died (64%), while in moderate category 56 out of 103 patients died (54%). POP Score and it's relationship with ventilator requirements and mortality as per statistics are very significant (p value are <0.0001).

Table 1: POP score and it's relation with ventilator support required and mortality

POP SCORE	NO.OF PATIENTS (in percentags)	VENTI SUPPORT (in percentags)	EXPIRED (in percentags)
0-3 (MILD)	35(24%)	7 (19%)	5(14%)
4-7 (MODERATE)	103(69%)	95(92%)	56(54%)
8-11 (SEVERE)	12(7%)	12(100%)	7(64%)
TOTAL	150(100%)	113(75%)	68(45%)

Based on Proudfoot classification, mild OP toxicity is defined as less than 10% reduction of PChE activity , moderate toxicity as 10-50% reduction and severe toxicity as >50% of reduction. In keeping with this definition, we have classified the patients and results were recorded as tabulated below. Statically significant correlation found for ventilator support and PChE level (p value < 0.0001) but no significance found with mortality (P value-0.08).

Table 2: Cholinesterase and it's relation with ventilator support required and mortality

S.Che LEVELS	NO.OF PATIENTS (in percentags)	VENTI SUPPORT (in percentags)	EXPIRED (in percentags)
<100 (SEVERE)	104(69%)	89(86%)	54(52%)
100-200 (MODERATE)	25(17%)	17(68%)	9(36%)
200-400 (MILD)	14(9%)	3(21%)	3(21%)
>400 (NORMAL)	7(5%)	4(57%)	2(29%)
TOTAL	150(100%)	113(75%)	68(45%)

Considering adult CPK reference Range as 46-171 U/L for male and 34-145 U/L for female, We classified the patients into mild, moderate and severe as tabulated below. Statistically we found good correlation between CPK level and ventilator requirements and mortality (p value <0.0001).

Table 3: S.CPK and it's relation with ventilator support required and mortality

S.CPK LEVEL	NO.OF PATIENTS (in percentags)	VENTI SUPPORT (in percentags)	EXPIRED (in percentages)
<200 (NORMAL)	65(43%)	29(45%)	5(8%)
200-400(MILD)	28(19%)	27(96%)	18(64%)
400-600 (MODERATE)	15(10%)	15(100%)	12(80%)
>600 (SEVERE)	42(28%)	42(100%)	33(79%)
TOTAL	150(100%)	113(75%)	68(45%)

DISCUSSION

OP insecticides are arguably one of the commonest causes of morbidity and mortality due to poisoning worldwide, especially in developing countries like India. The morbidity and mortality outcome depends on time lag between exposure and the onset of management. With increase in use of OP compounds for agricultural and industrial purposes and due to easy access and low cost, they are becoming a major source of health hazard. So, it

is cardinal to recognize the entire spectrum of the symptoms. Identification, risk stratification, early diagnosis and prompt treatment of OP poisoning victims are equally vital.

Symptoms are classified into muscarinic and nicotinic based on the receptor involved. Muscarinic features include excessive salivation, lacrimation, urination, diarrhea, gastrointestinal cramps, emesis, blurred vision, miosis, bradycardia, and wheezing. Nicotinic features

include fasciculation, paresis or paralysis, hypertension and tachycardia. Central receptor features include anxiety, confusion, seizures, psychosis and ataxia. Three types of paralysis are noticed. Type I is due to continued depolarization at neuro-muscular junction, type II due to intermediate syndrome and type III due to delayed polyneuropathy.

In 1993, Nimal Senanayake, H.J. de Silva and Lakshman Karalliedde[8] have developed a clinical scale to assess severity of organophosphorus (OP) intoxication. Five common clinical manifestations of OP poisoning have been selected as parameters, each 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. The scale was validated using two consecutive series of total 173 patients with OP poisoning. Correlations between the scores obtained on admission and three outcome variables, namely, death, the need for ventilatory support and the dose of atropine required in the first 24 hours after admission were significant. They conclude that this scale would assist in grading severity of OP intoxication at first contact and help in predicting possible outcome. Here, in our study, we have classified our study patients according to this POP scale and statistical significance was calculated. We found strong correlation between various score level and mortality and ventilatory requirements (p-value = 0.0001).

Though there has been controversy regarding prognostic Use of Plasma Cholinesterase (PChE) estimation in OP poisoning^{9,10}, we have found statistically significant correlation between various levels of PChE and ventilatory requirement. Similar findings are there in studies conducted by Mehta *et al*¹¹ in 1970 where they found lower activity of PChE in more than 70% of cases at presentation. Goswamy *et al.*, in their study concluded that apart from clinical indicators, low serum cholinesterase levels were of greatest predictive value for ventilation in OP poisoning¹².

The presence of muscle fiber necrosis in OP poisoning has been already demonstrated in animal experimental studies by Calore *et al*¹³. Because of this reason, studies regarding Creatine Phosphokinase (CPK)- A muscle enzyme, in organophosphorus poisoning had started. We also observed that serum CPK level was elevated in OP compound poisoning. Amount of rise depends upon the severity of poisoning. There was strong positive correlation between the clinical severity of poisoning and initial levels of serum CPK. In our study, the association between serum CPK levels and severity of organophosphorus poisoning according to POP score was statistically significant (P value <.0001). Similar results

were observed in the studies done by K.Bhattacharya *et al*¹⁴, Nermeen *et al*¹⁵ and D. Markandeyulu *et al*¹⁶.

Acidosis is a frequently encountered complication of OP poisoning, and it was previously suggested that both the degree and type of acidosis can be a predictor of outcome in OP poisoning¹⁷. It is documented that acidosis itself can cause modest elevations in CPK levels in blood, which implies that CPK can be falsely high in case of acidosis¹⁸. Serial measurements of CPK are required to predict the occurrence of intermediate syndrome - not an uncommon complication. These two things are lacking in our study because of limited resources. This can be considered as limitations of our study. Other newer markers apart from Plasma cholinesterase and serum CPK, are serum amylase and serum albumin levels. In organophosphorus poisoning raised serum amylase (hyperamylasemia) level is secondary to pancreatic injury because of parasympathetic overstimulation and hypersecretion. There have been studies showing that elevated serum amylase on the day of admission was related to the development of respiratory failure and further need for ventilatory support and increased mortality¹⁹.

CONCLUSION

On the basis of above study findings, we are concluding that POP score should be used as a primary tool in all Organophosphorus poisoning particularly at primary health centres where it will be helpful in judging severity of patients and in deciding timely regarding further referral of the patients which may need ventilatory support. We also recommend to go for serum CPK level along with plasma cholinesterase level to decide prognosis of patients as our study suggests good significance of them with ventilatory requirements and mortality with them.

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