

STUDY OF LEVELS OF SERUM CREATINE PHOSPHOKINASE AND LIVER ENZYMES AS A PROGNOSTIC INDICATORS IN ACUTE ORGANOPHOSPHORUS POISONING

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ABSTRACT

Background: Organophosphorus (OP) poisoning is one of the most common poisoning in rural and in developing country. Due to their easy availability and cost effective it is used frequently for homicidal and suicidal attempts. Routinely used biochemical markers like Erythrocyte cholinesterase (EChE) and Plasma cholinesterase (PChE) are used for the diagnosis of acute organophosphorus (OP) poisoning but estimation of these are very costly and not easily available. The mortality increases with increase in initial creatine phosphokinase level and can be used as alternative biomarker. Hence study was done to estimate levels of serum Creatine Phosphokinase (CPK) and liver enzymes in acute OP poisoning patients and its prognostic significance. **Methodology:** Patients (80) admitted in our hospital were included in this study. A brief history and detailed clinical examination was performed and patients were categorized on the basis Modified Dreisbach's clinical criteria classification. Serum levels of Creatine kinase (CK) and Liver enzymes were analysed at the time of admission. The outcome of the patients were observed. **Results:** Out of 80 patients recruited for the study, 41 cases (51.3%) were females, and 39 cases (48.8%) were males. Majority of them were in the age group of 21-30 years. More cases of OP poisoning were among agriculturalists 28 (35%) and housewife 21 (28.8%) and among students 15 (18.8%). Malathion was the most common compound used followed by Monocrotophos. 60% had mild, 31.3% had moderate and 8.8% had severe poisoning. There is increase in Creatine Phosphokinase (CPK) levels in 6 patients who survived with ventilator support and also in 2 patients who died with ventilator support which was statistically highly significant ($p < 0.05$). Serum liver enzymes were within normal limits. **Conclusion:** Elevated Creatine kinase is commonly seen in OPC poisoning. High initial serum Creatine Phosphokinase (CPK) levels are associated with severe degree of poisoning and are associated with complications and mortality. Serum liver enzymes (SGOT AND SGPT) are not elevated in OP poisoning.

Keywords: OP compound; Creatine kinase; Liver enzymes; respiratory failure.

INTRODUCTION

Organophosphorus (OP) insecticides are arguably one of the common causes of morbidity and mortality due to poisoning worldwide especially in developing countries like India. The morbidity and mortality depends on the time lag between the exposure and the onset of management.[1] According to the World Health Organization (WHO), 1 million serious unintentional poisonings occur every year and an additional 2 million people are hospitalized for suicide attempts with pesticides. Acute poisoning by Organophosphorous Pesticides (OP) has reached epidemic proportions in most parts of the world, particularly in developing agrarian countries, where the toxicity of available poisons and paucity of appropriate medical facilities results in a high fatality

rate.[2,3] Organophosphorous compounds are principally used as pesticides, and their exposure is highly prevalent in developing countries. In India use of insecticides accounted for 67% of the total pesticide consumption in 2006. The potential adverse impact on human health from exposure to pesticides is likely to be higher in countries like India due to easy availability of highly hazardous products and low risk awareness, especially among children and women. Overexposure to pesticides can occur before spraying because of easy access for children, lack of adequate labeling and during mixing, during spraying and after spraying operations. Spray operators and bystanders can be affected. Suicidal poisonings are common as pesticides are cheap and easily available in market.[4] The number of cases of pesticide poisoning in India annually has been estimated to be 76,000 [4]. Furthermore, Gunell et al, 2007 calculated that the number of intentional OP poisoning cases are 1,26,000 annually. These pesticides are misused as an important commodity for deliberate self-harm in developing world.

These OP compounds inhibit the acetylcholinesterase



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enzyme leading to accumulation of acetylcholine. The accumulated acetylcholine has effects on both muscarinic and nicotinic receptors at the synapses within the central and peripheral nervous system. There are several systems of grading of severity in acute organophosphorus poisoning. We used Modified Dreisbach clinical criteria to classify the subjects as mild, moderate and severe based on clinical presentation and after that we compared these subjects with their initial Creatine Phosphokinase (CPK) and liver enzymes level (SGOT and SGPT) and correlated with severity of poisoning [5].

Determination of PChE activity in blood has remained a mainstay and gold standard method for the initial screening and establishment of early diagnosis but it does not correlate with the severity of poisoning and cannot be used as a prognostic indicator. Estimation of serum creatine kinase and liver enzymes like SGOT and SGPT, serum amylase has become one of the new emerging options in predicting the severity of OP poisoning[6]. Estimation of Creatine Phosphokinase (CPK) is easy and levels are increased both in acute phase and in intermediate syndrome due to muscle fibre necrosis.

This study was aimed at evaluating the levels of serum creatine kinase (CPK) and liver enzymes (SGOT and SGPT) and its clinical significance in acute Organophosphorous poisoning (OP).

AIMS: To assess serum Creatinekinase and liver enzymes levels in OP poisoning and its prognostic significance.

MATERIALS AND METHODS

Study design: A prospective observational study

Ethics approval: The study was approved by the institutional ethics committee and informed consent was obtained from patient/guardian

Study location: Department of Medicine, Shri B M PATIL Medical College and Research Hospital vijayapura

Study duration: Study was conducted from November 2015 to June 2017.

Sample size: 80 patients with acute Organophosphorus poisoning

Inclusion criteria: All patients with a history of consumption and/or exposure of OP poison of either sex admitted to hospital within 12 hours of ingestion and not having been treated outside.

Exclusion criteria: Patients with indication of exposure to entirely different poison other than OP poison or mixed with any other poison, chronic alcoholics, chronic liver disease, History suggestive of myopathy, malignancy, autoimmune diseases, renal disease, drugs like Statin, Fibrate, Dexamethasone are

excluded from the study.

STUDY PROTOCOL: Patients admitted in SHRI B M PATIL MEDICAL COLLEGE AND RESEARCH HOSPITAL were the study group. Qualifying patients were subjected for detailed history, clinical examination and biochemical examinations. Admissions were always through the emergency department where initial decontamination procedures were carried out. A detailed clinical examination was carried out with particular reference to vital parameters, pupil size, assessment of all the others systems as per prescribed proforma. This examination took place during initial presentation and the cases were followed up during treatment of the patients. Modified Dreisbach clinical criteria was applied to all the study subjects and the severity of OP poisoning was graded as mild, moderate, severe at the time of admission.

Sample collection: In all the study subjects, 3ml of blood was drawn on admission before administration of atropine, plasma cholinesterase and serum creatine phosphokinase and liver enzymes were estimated. Serum creatine phosphokinase (CPK) was estimated by kit provided by BioSystems reagents and instruments using Erba Mannheim semi auto analyser, Serum cholinesterase (SCE) was estimated by colorimetric method by kit provided by Radox laboratories LTD. Liver enzymes (SGOT AND SGPT) estimated by using biosystem analyser.

Statistical analysis: Data were analyzed using Microsoft office and later SPSS software v.23.0. Using this software, frequencies, percentages, means, standard deviations, Chi-square and 'p' values were calculated. Kruskal Wallis chi-square test was used to test the significance of difference between quantitative variables and ANOVA and F test for qualitative variables. A 'p' value less than 0.05 is statistically significant.

RESULTS

A total of 662 patients with poisoning were admitted to our hospital during the study period and among them 295 cases were Organophosphorus compound detected and 80 patients were included in the study after applying inclusion and exclusion criteria. Majority of the patients were in the age group of 21-30 years which comprised 38.8% (31cases) of the study population. 23.8% (19 cases) of patients were in the age group of <20 years and minimum age group is 15 years and maximum age is 58 years respectively. In our study 51.3% (41cases) were females and 48.8% (39 cases) were males with M/F ratio 0.95.

Incidence of OP poisoning cases was more in agriculturist 35% (28 cases) and with rural background comprising of 61.3% (49 cases). Common mode of exposure is through oral.

In our study, the most commonly consumed compound

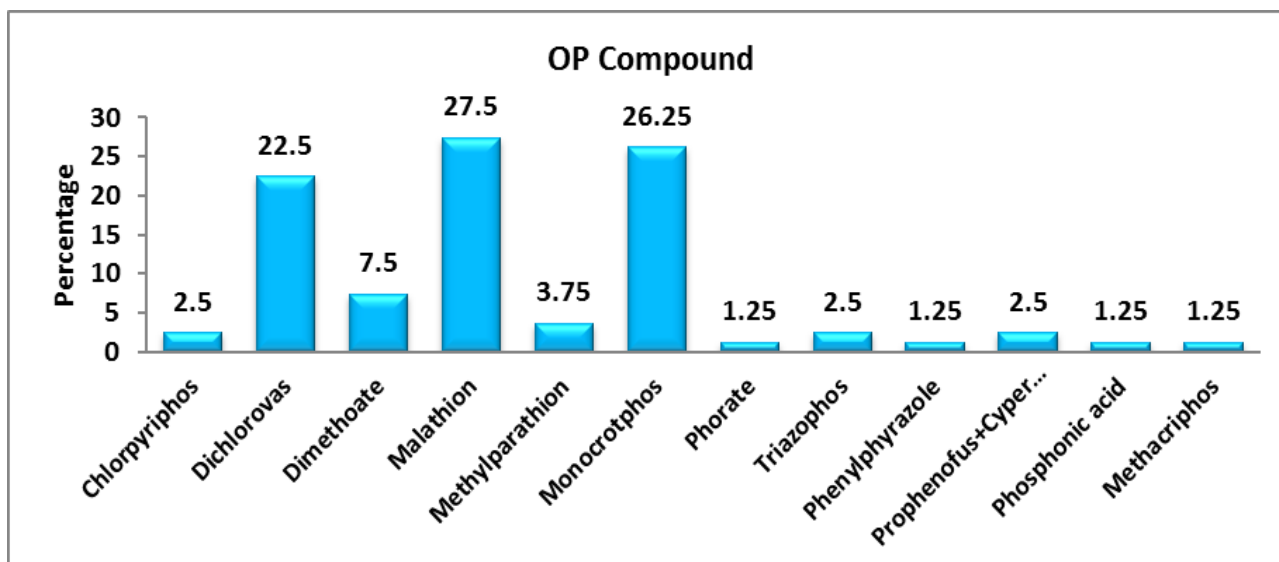


Figure 1: Distribution of cases according to OP Compound

Table 2: Association of Dreisbach’s Classification and mean biochemical prognostic parameters

Parameters	Mild Mean±SE	Moderate Mean±SE	Severe Mean±SE	ANOVA p value
SCE (IU/L)	4144.1±500.2	2743.2±346.1	1727.5±977.0	0.003*
CPK TOTAL(U/L)	221.9±29.4	273.1±74.2	641.9±256.1	0.008*
SGOT (U/L)	24.8±1.6	27.8±4.3	72.1±22.5	0.001*
SGPT (U/L)	19.3±1.4	21.50±11.1	69.1±18.2	<0.001*

Note: *means significant at 5% level of significance (p<0.05)

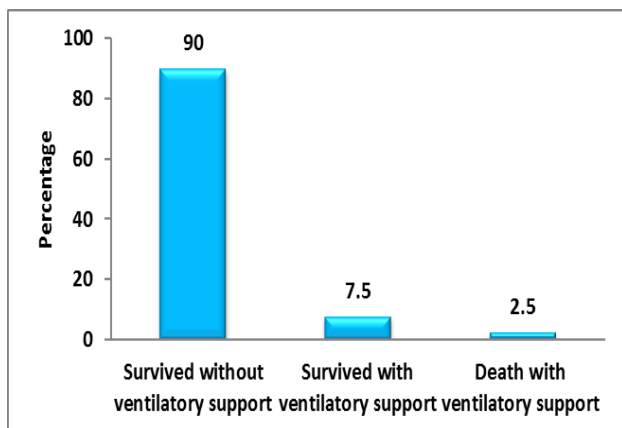


Figure 2. Distribution of cases according to clinical outcome

was malathion 22 patients (27.5%) followed by monocrotophos 21 patients (26.25%) and 18 patients (22.5%) were consumed dichlorovas (Figure 1).

Out of 80 patients under study, 72 patients which accounts for 90% have survived without ventilatory support and 6 patients 7.5% have survived with ventilatory support and 2 cases 2.5% of patients died with ventilatory support (Figure 2).

Table 1. Distribution of cases according to Dreisbach’s Classification

Dreisbach’s Classification	N	%
Mild (grade I)	48	60
Moderate (grade II)	25	31.3
Severe (grade III)	7	8.8
Total	80	100

Modified Driesbach’s criteria is used to classify the severity of poisoning in our study. 48 patients out of 80 cases (60%) were in clinical severity grade 1 and 25 patients (31.3%) in clinical severity grade 2 and 7 patients (8.8%) in clinical severity grade 3 respectively (Table 1).

The mean CPK levels in mild, moderate and severe poisoning were 221.9, 273.1 and 641.4 respectively. It was found to be statistically significant. The mean liver enzymes (SGOT and SGPT) levels mild and moderate poisoning were found to be normal limits (Table 2).

DISCUSSION

In India, the most common used pesticide in agriculture is Organophosphorus compound and it has become one of the major health issues especially in developing countries because of their easy availability and wide use of pesticides.[7] In our study, the incidence of OP poisoning is higher in the age group of 21-30 years (38.8%), followed by 23.8% in the age group 11-20 years. This is consistent with the study done by Bhattacharyya et al[8] which showed that most commonest age group is 21-30 years and also in Mcihammet G et al[9]. But in the study done by Hassan NAM et al[10] the common age group is 11-20 years. As we can see the most common group of affected individuals are among youngsters and the reason may be because these individuals are vulnerable to various emotion conflicts that occur during this phase of life. Majority of the patients in our study were females which accounting for 51.3% 41 cases and males were 39 cases 48.8%. This is consistent with Murat S et al[11] study with female predominance and also in the study done by Hassan NAM et al[10] with 51.7% were males and 48.3% were males. But in Bhattacharyya et al[8] study 66.6% were males and 33.3% were females.

The commonest mode of poisoning was suicidal in nature. This accounts for 98.8% in our study and most common route of exposure was oral route. This is similar with the study done by Murat et al[11]. In our study, majority of OP poisoning were among farmers (35%) and most of them were illiterates (63.8%).

India is an agrarian country with around 70% of the people depending directly or indirectly upon agriculture with higher incidence of OP poisoning is seen in rural areas than in urban population which accounts for 61.3 % and 38.8%. This is consistent with Dalal et al[12] and Otto et al[13] respectively.

The most common compound used in our study is Malathion and Monocrotophos 27.5% each followed by Dichlorvas 16.3%. In study done by Murat et al[11] Dichlorvas was commonest compound where as in Karaliedde L et al[14] study dimethoate was common compound consumed among OP patients.

The mean pseudocholinestrase levels in mild, moderate and severe poisoning cases were 4144.1, 2743.2 and 1727.6 respectively. The mean CPK levels in our study in different grades of poisoning were 221.9, 273.1 and 524.4. These CPK levels are similar with the study conducted by Bhattacharyya et al[8], Sen R et al[1], Eun-Jung Kang, Su-Jin Seok , Kwon-Hyun Lee et al[15], Kale BS et al[16], Vijayakumar PG et al[17], Eizadi Mood N et al[18] respectively.

Our study revealed that changes in serum creatine kinase and its raised level were associated with (6 patients) respiratory failure and (2 patients) death. 4 out

of 21 patients with moderate poisoning required ventilator support and 2 of 7 patients with severe poisoning required ventilator support. Early onset respiratory failure is seen within 24 hours of exposure in 5 patients this may be due to cholinergic over activity such as increased salivation, increased sweating, increased bronchial secretions, pinpoint pupil, depressed level of consciousness and respiratory failure.

Only 1 patient had late onset respiratory failure i.e after 24 hours of exposure this may be attributed to respiratory infection. Average arterial blood gases values of these patients were P^H - 7.24 (range 6.98-7.40), Pco_2 -40.6mmhg (range 20-51mmhg), Po_2 -68.6(50-98mmhg), Hco_3 -14.4(range 10-24mmol/l), Sao_2 - 88.6% (range 84-98). The duration of mechanical ventilation was 6.2 ± 7.4 days.

2 patients with mechanically ventilated in severe poisoning died of cardio respiratory arrest following myocardial infarction and pneumonia and their abnormal laboratory values were elevated liver, renal and cardiac enzymes with hyperglycemia and elevated triglycerides. Total duration of all the respiration failure patients were 16.6 ± 7 days.

In our study patients who developed respiratory failure their initial CPK level were above 250 and patient who died, their CPK levels were 1441 and 1116 which is consistent with the study done by Bhattacharyya et al[8]. High serum levels of creatine kinase at admission indirectly indicated the severity of poisoning and these correlations are found to be statistically significant. We also found that high initial CPK level is associated with higher rates of respiratory failure requiring endotracheal intubation and mechanical ventilation and higher mortality.

In the present study mean levels of liver enzymes are within normal range in cases without complications as well as cases with respiratory failure and deaths. There is no much increase in liver enzymes in these groups. This is consistent with the study done by AB Patel et al [19] and there is slight impairment of the liver enzymes in a study done by Antonio F Fernandez et al[20] but overall these findings are consistent with no clinical significant hepatotoxicity.

In our study, we found that high initial serum creatine kinase levels (CPK) is associated with severe degree of poisoning and is associated with complications and mortality and the results were statistically significant.

Complications like respiratory failure in 6 patients, pneumonia in 3 patients, acute kidney injury in 2 patients, convulsions in 1 patient and myocardial infarction in 1 patient.

CONCLUSION

Serum creatine kinase should be used as an alternate

biomarker and considered as a routine investigation in order to predict the respiratory failure and its outcome of OP poisoning severity.

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