

Original Research Article

Creatinephosphokinase in organophosphorus poisoning

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ABSTRACT

Background: Organophosphorus Poisoning has been found to be a major cause of death or morbidity in our country as it freely available without need of prescription unlike in developed countries where prescription is required to purchase insecticides, the various organophosphorus compounds available are Malathion, parathion, diazinon, fenthion, dichlorvos, chlorpyrifos, ethion. Erythrocyte cholinesterase (EchE) and pseudocholinesterase (Butyryl cholinesterase-BchE) are markers used for assessing the severity in OP poisoning, but estimation of these are costly, has variable values for different individuals and is not available at all centers. This study was done to estimate levels of serum Creatine Phosphokinase (CPK) serially in acute OP poisoning patients and to correlate with prognosis.

Methods: 50 patients of organophosphorus poisoning admitted to Mcgann hospital attached to Shimoga institute of medical sciences Shimoga over a period of 6 months from 1st July 2016 to 31st December 2016 were taken up for the study. A comprehensive history and detailed clinical examination was performed and patients were clinically evaluated for severity. Level of serum cholinesterase and serum CPK were estimated at admission and CPK level was measured on day 3 and day 5. The outcome of these patients was evaluated.

Results: Out of 50 patients, 78% (n=39) were males and 22% (n=11) were females. Majority of patients were in the age group 21 – 40 years. Chlorpyrifos was the most common compound used. 72% had mild, 20% had moderate and 8% had severe poisoning. Serial measurements of serum CPK levels showed significant correlation with the severity of acute OP poisoning patients. The CPK levels showed a sensitivity of 74% and a specificity of 81% with a positive predictive value of 92%.

Conclusions: Severe organo phosphorus poisoning is correlated with CPK levels. This study recommends CPK level estimation in assessment of severity and prognosticate patients with organophosphorus compound as alternate marker to choline esterase.

Keywords: Creatine phosphokinase, OP compound

INTRODUCTION

Organophosphorus compounds are protease and serine esterase inhibitors, widely used as insecticides in agriculture. It's a major contributor of poison associated morbidity and mortality in our country. The World Health Organization estimates based on 2001 data, revealed 8,49,000 deaths across the world from attempt to end life each year.¹ The incidence is higher in adolescent and young people, in developing countries, with mortality

rate ranging from 10 to 20%.² Occupational exposure to the organophosphorus compound accounts for about 20% of patients with mortality about 1%. Accidental poisoning accounts for 8-10% of the incidents and homicidal use (< 1%) were other forms of poisoning.^{3,4}

Organophosphorus compound act by inhibiting the acetylcholinesterase enzyme (AChE) at muscarinic and nicotinic receptors, producing a group of symptoms like papillary constriction, low heart rate, increased gastrointestinal motility, vomiting, profuse sweating,

respiratory distress, salivation, lacrimation, altered sensorium, fasciculation, bronchospasm, blurred vision, photophobia, urination and defecation. The major complications associated with organophosphorus compound poisoning include acidosis, respiratory paralysis, acute renal failure, seizures, arrhythmias, aspiration, coma and even death. Furthermore, these insecticides increase reactive oxygen species level which results in oxidative stress that contributes to cell membrane lipid peroxidation, DNA damage and cell death.^{5,6}

Laboratory evidence of OP poisoning is usually confirmed by measuring the decreases in the blood and erythrocyte cholinesterase activities. However, because of wide inter-individual variability and also the cost factor the serum EChE or BChE levels are not routinely performed.⁷ There are emerging options for newer economically viable and easily quantifiable biochemical markers in relation to OP poisoning like creatine phosphokinase (CPK), lactate dehydrogenase (LDH) and serum immunoglobulins (IgG, IgA).⁸ As of today only very few studies has shown that serum cholinesterase (ChE) and CPK level estimations are useful in diagnosis of organophosphorus poisoning in acute phase.^{9,10} Hence, this study was planned for assessing CPK as a diagnostic and prognostic marker in patients with acute organophosphorus compound poisoning.

METHODS

A total of 50 patients of OP poisoning who were admitted to Mcgann Hospital, attached to Shimoga institute of medical sciences, Shimoga were included in the study after taking written informed consent. Patients with chronic liver disease, myopathies, chronic kidney disease, seizure disorder, receiving intramuscular injection, cardiopulmonary resuscitation, and trauma were not included in the study. Confirmation of OP poisoning was done by seeing the container brought along with patient by attenders.

All the patients were categorized according to severity determined by clinical examination as mild, moderate and severe. Patients who had consumed or exposed to Organophosphorus compound were managed as per the international guidelines with initial atropine bolus 2 mg followed by double doses of bolus every 5 minutes till the signs of atropinization appeared. The initial bolus was followed by 2mg/hour infusion. PAM was given to all patients in the dose of 500mg to 1g intravenously every 6 hours depending on the body weight. All patients underwent comprehensive evaluation for severity and prognosis determined. Blood samples were collected by a single prick aseptic method for serum CPK on day of admission and on day 5 using spectroscopic methods along with routine blood evaluation. The data thus obtained was analysed using Chi-square and Unpaired Student t-test and SPSS software.

RESULTS

The age and sex wise distribution of the entire study subjects was shown in Table 1. It is seen from the table that in both the male and female groups majority of the study subjects were in the age group of between 20 – 30 years. Of the entire study subject's males were more in numbers than the females. Among the various poisons consumed by the study subjects chlorpyrifos (50%) and Monochrotophos (34%) were the most common form of Organophosphorus poison as depicted in Table 2. The other forms of OPC poison consumed by the study subjects were 2% methyl parathion, dimethaote, quinolphos etc. The severity of the OPC poisoning was assessed by clinically. Parameters which were taken into consideration like pupil size, respiratory rate, heart rate, fasciculations, level of consciousness and seizures. In the present study the mild form (72%) of OPC poisoning was most common followed by moderate (20%) and severe form (8%) (Table 3). The enzymes that were measured in the patients who had consumed OPC poison were serum cholinesterase, and CPK. It is concluded from the study that there was a very strong positive correlation between CPK and severity of poisoning. The CPK levels can also be used in classifying the severity of OPC poisoning. In the study subjects the CPK levels were lower in milder form of poisoning when compared to the moderate and severe form where CPK levels are high and is found to be statistically significant.

Table 1: Age wise distribution of cases.

Age group	Male	Female	Total
<20years	12	2	14
20-30 years	15	6	21
30-40years	9	1	10
40-50years	2	1	3
>50years	1	1	2
Total	39	11	50

Table 2: Distribution of various OP compounds in poisoning.

Type of poison	Number of patients	%
2% methyl parathion	04	8
Chlorpyrifos	25	50
Monochrotophos	17	34
Dimethoate	01	02
Profenophos	01	02
Quinolphos	01	02
Triazophos	01	02

In our study the majority of cases 72% (36 cases) belonged to mild severity followed by 20% (10 cases) moderate severity and 8% (04 cases) were most severe according to clinical parameters described in the study. The mean duration of hospital stay was 6.8 days. The mortality was higher among cases with more severe type of poisoning.

Table 3: Percentage cases based on severity.

Clinical grade	Cases	%
Mildly severe	36	72
Moderately severe	10	20
Most severe	04	08

In our study out of 50 cases studied, 76% (n=38) had creatine kinase < 180 IU/L while 24% (n=12) had values of creatine kinase >180 IU/L. On comparing 2 groups, group with lower CPK at admission 80% (n=40) improved in group I whereas 12 % (n=6) of cases improved in group II which had higher CPK levels. Only 4% (n=2) cases had respiratory depression in group I compared to 50% (n=3) in group II. The mortality in group I was 4% (n=2) compared to 25% (n=12) in group II. Higher mortality was observed in cases with higher creatine kinase compared to cases with lower creatine kinase values. This was found to be statistically significant.

Table 4: Outcome of patients depending on CPK value.

Creatinekinase	Improved	Respiratory failure	Death	Total
<180 IU	34	2	2	38
>180 IU	6	3	3	12

DISCUSSION

Our study has shown that serum Creatinephosphokinase levels are comparable to cholinesterase in prognostification of patients with acute organophosphorus poisoning. p value is statistically significant ($p < 0.05$). Studies have shown that when a skeletal muscle is injured, CPK leaks into the circulation and excreted in urine. Serum CPK is the best diagnostic investigation for assessing skeletal muscle damage. Elevation of serum CPK levels in acute organophosphorus compound poisoning more so in severely poisoned is due to muscle fiber necrosis.¹¹

These results are in agreement with Bhattacharyya et al who observed close correlation between initial CPK value and severity of poisoning.¹² Muscle fiber damage occurs in the form of necrosis and thereby causes elevated CPK in acute organophosphorus poisoning. This study has demonstrated that CPK is easily available, easy to process and easily quantifiable alternative biomarker in patients with acute organophosphorus poisoning. CPK estimation is also valuable clinical biomarker for prognostification of severity. The disadvantage of serum CPK as a biomarker for acute organophosphorus compound poisoning is its nonspecificity. Other conditions like liver cell failure, muscular dystrophies should be excluded before concluding on severity. Sniderman et al stated that many factors have influence on CPK activity, so the suitability of CPK as a biomarker for diagnosis of muscle injury and disease should be viewed with caution.¹¹ Also, researches illustrated that

there are multiple causes of elevated CPK, which may affect its reliability as a biomarker.

CONCLUSION

Organophosphorous poisoning is most prevalent in the age group of 21-30 years. Incidence of organophosphorus poisoning is more common in males. Severity of organophosphorus compound is easily prognosticated by serum CPK levels. Higher levels of CPK closely correlated with more severe disease. The elevation of CPK levels is predictive of subsequent respiratory failure. Early estimation of Creatine Kinase should be routinely considered as it is a good prognostic marker.

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