Creatine Kinase for Prognostication in Organophosphorus Poisoning

Dayanand Raddi¹, Anikethana G V²

¹,²Postgraduate Student, Department of General Medicine, Karnataka Institute of Medical Sciences, Hubli, Karnataka, India – 580022

Abstract: Organophosphorus poisoning is the responsible for a significant morbidity and mortality in agrarian countries. The incidence of poisoning is higher in young, economically active group with a fatality rate of 10-20%. Our study was done to evaluate the prognostic significance of Creatine kinase in organophosphorus poisoning. During the study period a total of 360 poisoning cases were admitted to the hospital of which 80 were eligible for the study. The morality in patient with elevated creatine kinase was 39.47% as against 4.76% in patients with normal creatine kinase. It was statistically significant. Ventilator requirement in patients with elevated creatine kinase was statistically significant (44.74% vs 9.52%). The study emphasizes the role of creatine kinase in prognostication of patients presenting with organophosphorus poisoning.

Keywords: creatine kinase, organophosphorus poisoning, acute poisoning, severity of poisoning, modified Dreisbach criteria

1. Introduction

Organophosphorus compounds are serine esterase and protease inhibitors, widely used in agriculture as insecticides. Toxic effects of organophosphorus compound are associated with significant morbidity and mortality making it a major global clinical problem. The World Health Organization estimates based on 2001 data, revealed 8,49,000 deaths across the globe from self-harm each year. The incidence is higher in young, economically active group, in developing countries, with a case fatality rate of 10-20%. Poisoning due to occupational exposure accounted for about one fifth of the incidents, with a fatality rate of less than 1%. Accidental exposures accounted for 8-10% of the incidents and homicidal use (< 1%) were other forms of poisoning.

The importance of pesticides in India can be understood from the fact that agriculture is a major component of the Indian economy. 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, where the toxicity of available poisons and paucity of appropriate medical facilities results in a high fatality rate.

The pathological effects of organophosphates result from inhibition of cholinesterase (both RBC and pseudocholinesterase). These are the markers of exposure, acute toxic effects and reflect actual activity at cholinergic nerve terminal. In the acute phase of organophosphorus poisoning serum cholinesterase activity is usually depressed within a few hours to few days and is also restored to normal levels quickly.

Case reports on clinical significance of creatine kinase in acute organophosphorus compound ingestion has been reported now and then, but there are no large-scale studies with reference to clinical significance of creatine kinase. Hence an attempt will be made to study clinical significance of creatine kinase in organophosphorus poisoning, which might help in early recognition, prognostication and optimal utilisation of resources.

2. Aims and objectives

To study the changes in serum levels of creatine kinase in cases with organophosphorus compound poisoning and its prognostic value.

3. Materials and methods

Cases of organophosphorus poisoning presenting to the Karnataka Institute of medical sciences within 12 hours of consumption and age >18 years between the period of December 2011 and November 2012 was included in the study. Patients with chronic alcoholism, chronic liver disease, and chronic renal disease, history suggestive of myopathy or history of intake of statins, fibrates or dexamethasone were excluded.

Data was collected using a preformed proforma from each patient. The diagnosis of organophosphorus poisoning was based on history, clinical examination or response to treatment with atropine. The routine biochemical investigations including creatine kinase was obtained. Statistical analysis was done using SPSS 17.0 software. The significance was tested using Chi-square test and ‘p’ values.

4. Observation and Results

A total of 360 cases of poisoning was admitted during the study period. After applying inclusion and exclusion criteria, 80 cases were eligible for study. Out of 80 cases studied, 45% (36) cases were in the 21 to 30 years age group, 16.25% (13) cases were in 31-40 year age group and 17.5% (14) cases were in below 20 year age group. The majority of cases 61.25% (49) were between the age group 20 to 40 years. Out of 80 cases recruited for the study, 58.75% (47 cases) were males, and 41.25% (33 cases) were females. Incidence of organophosphorus poisoning was more in males when compared to females in our study.
Table 1: Distribution of cases according to severity of poisoning

<table>
<thead>
<tr>
<th>Clinical grades</th>
<th>Number of cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade I</td>
<td>20</td>
</tr>
<tr>
<td>Grade II</td>
<td>36</td>
</tr>
<tr>
<td>Grade III</td>
<td>24</td>
</tr>
<tr>
<td>Total</td>
<td>80</td>
</tr>
</tbody>
</table>

In our study the majority of cases 45% (36 cases) belonged to Grade II severity followed by 30% (24 cases) Grade III severity and 25% (20 cases) in Grade I. In our study maximum hospital stay was observed in 30% (24 cases) of cases having more severe poisoning (grade III), followed by grade II and grade I severity. The mean duration of hospital stay was 6.3 days. The mortality was higher among cases with more severe type of poisoning.

Table 2: Correlation of creatine kinase levels and outcome

<table>
<thead>
<tr>
<th>Creatine Kinase</th>
<th>Prognostic classification</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;180 IU</td>
<td>Improved</td>
<td>37</td>
</tr>
<tr>
<td>&gt;180 IU</td>
<td>Respiratory depression</td>
<td>7</td>
</tr>
<tr>
<td></td>
<td>Death</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>42</td>
</tr>
</tbody>
</table>

Pearson Chi-Square Value: 39.188 P Value: < 0.0001

In our study out of 80 cases studied, 52.5% (42 cases) had creatine kinase < 180 IU/L while 47.5% (38) had creatine kinase > 180 IU/L. On comparing 2 groups, only 18.4% (7/38) of cases improved in Group I compared to 88% (37/42) in Group II. Only 7.1% (2/24) cases had respiratory depression in Group I compared to 42% (16/38) in Group II. The mortality in Group I was 4.76% (2/42) compared to 39.4% (15/38) in Group II. Higher mortality 39.4% (15/38) was observed in cases with higher creatine kinase compared to 4.7% in Group I. These findings were found to be statistically significant.

Table 3: Correlation of Creatine kinase levels and ventilator need

<table>
<thead>
<tr>
<th>Creatine kinase</th>
<th>Ventilated</th>
<th>Total</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;180 IU</td>
<td>4</td>
<td>38</td>
<td>9.52</td>
</tr>
<tr>
<td>&gt;180 IU</td>
<td>17</td>
<td>50</td>
<td>44.74</td>
</tr>
</tbody>
</table>

Pearson Chi-Square Value: 12.8 P Value: < 0.001

Of the 42 cases with normal creatine kinase value, only 9.52% (4 cases) required ventilator support as compared to 44.74% (17 cases) with elevated creatine kinase value required ventilator support. This was statistically significant.

5. Discussion

Organophosphates and carbamates frequently used pesticides can result in serious morbidity and mortality with over 50,000 organophosphorous compounds have been synthesized since the first one by Clermont in 1857. The clinical symptoms range from the classic cholinergic syndrome to flaccid paralysis and intractable seizures, with mortality ranging from 10 to 22%. Efforts are being continuously made to find out better diagnostic, prognostic and therapeutic tools for better out come in such cases. Various studies have shown the significance of creatine kinase as prognostic factor, hence we conducted this study to analyze the same.

Present study included 80 cases in the age group of 18 to 70 years. The incidence of OP poisoning was higher in the age group of 21-30 years, (mean age being 25.07yrs). These are consistent with the findings of Guven MET ET AL where in a similar study the mean ages were 24.1 and 33.95 years in the age group of 21-30 years and 31-40 years respectively. Dassanayake T. ET AL of Srilanka documented that 91% of their cases were under the age of 30 years.

In our study group of 80 cases 58.75% (47 cases) were males, and 41.25% (33 cases) were females. These findings are consistent with, studies conducted by Sungur M ET AL (25 males, 51% and 23 females, 46%).

In our study, severity of poisoning was classified by using Modified Dreisbach Criteria. Out of 80 cases, most of the cases were in the Grade II group of clinical severity 47.2% (36 cases) followed by 27.77% (24 cases) in Grade III group and 25% (20 cases) in Grade I group. Arau KK ET AL reported, mild grade in 15 cases (14%), moderate in 55 cases (50.9%), and severe grade in 32 cases (29.6%). It was observed in our study that the severity of poisoning had proportionate relation with outcome, greater the severity poorer the outcome. The death rate incases with Grade I severity was 15%, Grade II was 16.6% and Grade III was 33.33%. These findings were consistent with the study conducted by Arup KK ET AL.

Many studies conducted by various authors have focused on correlation between levels of creatine kinase and clinical outcome among patients with organophosphorus poisoning. Among 80 cases studied we classified our patients into two groups. Group I consisted 52.5% (42/80) cases with creatine kinase value of < 180 IU, Group II had 47.5% (38/80) cases with creatine kinase value > 180 IU. The mean hospital stay duration among Group I was 3 days while it was 6.3 days in Group II. The clinical outcome in Group I with lesser creatine kinase value was better than Group II, in terms of survival and lesser complications. 44.74% (17 cases) of cases in Group II required ventilator as compared to 9.52% (4 cases) in Group I. The morbidity in terms of duration of hospital stay and need for ventilation and in Group II with higher creatine kinase values as compared to Group I with normal creatine kinase values. Mortality rate among Group II was 39.47% as compared to 4.7% in Group I. These findings were found to be statistically significant. These findings were consistent with the one’s reported in the literature that, initial increased creatine kinase values are associated with increased morbidity mortality and poor outcome in cases with organophosphorus poisoning.

Bhattacharya KET ALI in their study reported that initial creatine kinase activity was significantly elevated inorganophosphorus compound poisoning cases and more significant in cases with respiratory depression and expired cases. Agarwal S ET AL who reported that creatine kinase level was significantly elevated inorganophosphorus compound poisoning cases (p<0.01). Eizadi-Mood N ET AL in their study reported 75% of cases in high creatine
kinase level group, 29.5% in medium creatine kinase level group and 35% in low creatine kinase level group developed complication or death. They too observed that complications were much higher for cases with high admission creatine kinase levels than with low levels. Study concluded that the admission CPK level for poisoned cases seems to be an acceptable predictor for the outcome in poisoned cases. Vijayakumar PG et al. in their study reported that creatine kinase levels were elevated in organophosphorus compound poisoning cases. Significant creatine kinase levels were elevated in Grade II and Grade III poisoning cases. Which were associated with higher rates of respiratory depression and death. Similarly EJ Kang et al. showed that the creatine kinase activity was significantly elevated in organophosphorus poisoning cases and more significant alteration were observed in the cases who died due to poisoning indicating the cardiac functional impairment due to organophosphorus poisoning. It was presumed that the estimation of creatine kinase activity in suspected OP Poisoning cases may serve as corroborative diagnostic and prognostic parameter, alternative to cholinesterase. Study conducted by Kale B.S. also showed that creatine kinase levels were elevated in organophosphorus poisoning cases. In their study creatine kinase level significantly (p<0.01) correlated with severity of poisoning.

6. Conclusion

1. Organophosphorous poisoning is most prevalent in the age group of 21-30 years.
2. Incidence is more common in males.
3. The higher the clinical grade of poisoning at initial presentation, more is the incidence of respiratory failure and need for ventilator support.
4. Elevated Creatine Kinase is commonly seen in OPC poisoning. The elevation of CPK levels is predictive of subsequent respiratory failure.
5. Early estimation of Creatine Kinase should be routinely considered as it is a good prognostic marker.

References


Author Profile

Dr. Dayanand Raddi did MBBS from M S Ramaiah Medical College, Bangalore (2004-2010) and pursuing postgraduate course in MD (General Medicine) from Karnataka Institute of Medical Sciences, Hubli, Karnataka, India

Dr. Anikethana G V did MBBS from Mysore Medical College, Mysore (2003-2009) and pursuing postgraduate course in MD (General Medicine) from Karnataka Institute of Medical Sciences, Hubli, Karnataka, India