International Journal of Science and Research (IJSR)
ISSN (Online): 2319-7064
Impact Factor (2012): 3.358

Creatine Kinase for Prognostication in Organophosphorus Poisoning

Dayanand Raddi[1], Anikethana G V[2]

[1, 2]Postgraduate 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 case 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 mortality 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[1]. The incidence is higher in young, economically active group, in developing countries, with a case fatality rate of 10-20%.[2]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.[3],[4]

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.[5]

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.[6]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 creatinekinase in acute organophosphorous compound ingestion has been reported now and then, but there are no large-scale studies with reference to clinical significance of creatinekinase. Hence an attempt will be made to study clinical significance of creatine kinase in organophosphoruspoisoning, which might help in early recognition, prognostication and optimal utilisation of resources.[7,8,9,10,11,12,13]

2. Aims and objectives

To study the changes in serum levels of creatine kinase in cases with organophosphorus compound poisoning and it's 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 80cases recruited for the study, 58.75% (47 cases) were males, and 41.25% (33cases) 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

Clinical grades	*Number of cases*	
	Cases	*Percent*
Grade I	20	25
Grade II	36	45
Grade III	24	30
Total	80	100

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 %(24cases) of cases having more severe poisoning (grade III), followed by grade II and grade I severity. The mean duration of hospital stay was 6.3days. The mortality was higher among cases with more severe type of poisoning.

Table 2: Correlation of creatine kinase levels and outcome

Creatine Kinase	*Prognostic classification*			*Total*
	Improved	*Respiratory depression*	*Death*	
<180 IU	37	3	2	42
>180 IU	7	16	15	38
Total	44	19	17	80

Pearson Chi-Square Value: 39.188 P Value: < 0 .0001

In our study out of 80 cases studied, 52.5 % (42) 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 IIgroup compared to 88% (37/42) in group I. Only 7.1% (2/42) 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 4.76% (2/42) in cases with lower creatine kinase values. This was found to be statistically significant.

Table 3: Correlation of Creatine kinase levels and ventilator need

Creatine kinase	Ventilated	Total	Percent
<180 IU	4	42	9.52
>180 IU	17	38	44.74
Total	21	80	26.25

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

Of the 42 cases with normal creatine kinasevalue, only9.52% (4cases) required ventilator support as against 44.74% (17cases) 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%[14]. 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 21-30years, (mean age being 25.07yrs). These are consistent with the findings of GuvenMet al[15] 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[16]of Srilanka documented that 91% of their cases were under the age of 30 years. I

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 SungurM et al[17](25 males, 51% and 23 females, 46%).

In our study, severity of poisoning was classified by using Modified Dreisbach Criteria[18]. 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. Arup KK et al[19] 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[19].

Many studies conducted by various authors have focused on correlation between levels of creatine kinase and clinical outcome among patients with organophosphorus poisoning.[7,8,10,11]Among 80 cases studied we classified our patients in to two groups. Group I consisted 52.5% (42/80) cases with creatine kinase value of < 180 IU. Group II had47.5% (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.[7, 8,10,11,12,13]

Bhattacharya Ket al[7]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. AgarwalS et al[8] et al who reported that creatine kinase level was significantly elevated inorganophosphorus compound poisoning cases ($p<0.01$). Eizadi-Mood N et al[10] in their study reported 75% of cases in high creatine

kinaselevel 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 PGet al[12]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 Kanget al[13] 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.Set al[11]also showed that creatine kinase levels were elevated in organophosphorus poisoning cases. In their study creatine kinase level significantly ($p<0.01$) co-related 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 CreatineKinase is commonly seen in OPC poisoning. The elevation of CPK levels is predictive of subsequent respiratory failure.
5. Early estimation of CreatineKinase should be routinely considered as it is a good prognostic marker.

References

[1] The World Health Report 2002. Reducing the risks, promoting healthy life. WHO, Geneva; 2004.
[2] Jacobson D, Frederichsen PS, Knutsen KM, Sorum Y, Talseth T, Odegaard OR. Clinical course in acute self-poisoning: A prospective study of 1125 consecutively hospitalized adults. Hum ExpToxicol 1984; 3:107-16.
[3] Yurumez Y, Durukan P, Yavuz Y, et al. Acute organophosphate poisoning in university hospital emergency room cases. *Intern Med*. 2007; 46(13):965-9.
[4] Michotte A, Van Dijck I, Mals V. Organophosphorus Insecticide Poisoning. JIFCC 1999; 11 (2).
[5] CHS Rao, Venkateswaralu V, Surender T. Pesticide poisoning in South India: Opportunities for prevention and improved medical management Trop Med Int Health June 2005; 10(6): 581-588.
[6] Namba T. Cholinesterase inhibition by organophosphorus compounds and its clinical effects., Bull World Health Organ 1971; 44:289-307.
[7] Bhattacharyya K, Phaujdar S, Sarkar R, Mullick OS. Serum Creatine PhoshpoKinase: A Probable Marker of Severity in organophosphorus poisoning, ToxicolInt 2011 jul-dec; 18(2).117-123.
[8] Agarwal S, Bhatnagar V, Agarwal A, Agarwal U, Venkaiah K, Nigam S, Kashyap S. Impairment in Clinical Indices in Acute Organophosphate Insecticide Poisoning Cases in India. The Internet Journal of Toxicology 2007; 4(1).
[9] DA Khan, MM Bhatti,A Khan, ST Naqvi, A Karam. Adverse effect of pesticides residues on Biochemical markers in tobacco farmers ,Int j clinExp Med 2008; 1:274-282
[10] Eizadi–Mood N, Sabzghabaee AM,Gheshlaghi F, Mehrzad F, Fallah Z. Admission Creatine phosphoKinase in acute poisoning Is it a predictive factor? J PAK Med Assoc2012Mar; 62(3sppl 2);s67-70.
[11] Kale B.S. Creatine Kinase and LDH As Marker of Muscular Damage in Intermediate syndrome associated with Organophosphorous toxicity;Indian streams research journal 2012 Dec; 2(11).
[12] Vijayakumar PG,Samudram P,Rajendren C, Pregna B. Isoenzyme pattern of Creatine Kinase in Acute Organophosphorous Compound poisoning. Journal of the Indian Society of Toxicology 2011; 7(2).
[13] EJ Kang, SJ Seok, KH Lee, HN Gil, JD Yang, EY Lee, SY Hong. Factors for determining Survival in Acute Organophosphorous poisoning. Korean J Intern Med 2009 Dec;24(4);362-367
[14] Singh S, Sharma N. Neurological Syndromes, following organophosphate poisoning. Neurol Indian 2000; 48(4):308-13
[15] Guven M, Dogukan A, Taskapan H.Lcukocytosis as a parameter in Management of Organophosphate Intoxication Turk J Med Sci 2000; 30: 499-500.
[16] T Dassanayake, V Weerasinghe, U Dangahadeniya, K Kularatne, A Dawson, L Karalliedde, N Senanayake. Long-term event-related potential changes following organophosphorus insecticide poisoning.Clin Neurophysiology2008; 119:144-150.
[17] M Sungur, MGuiven. Intensive care management of organophosphate insecticide poisoning. Crit Care 2001; 5 (4)211-215
[18] Dreisbach RH. Cholinesterase inhibitor pesticides. In: Hand Book of poisoning 11th ed. Longe medical publications. California. 1983: 106-14.
[19] Arup KK et al. Predictors of mortality in Organophosphorus poisoning- Hospital based study from suburban West Bengal. JAPI. Vol 49, January 2001,59 page 91.

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