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Medicine

SERUM CREATINE KINASE: A MARKER OF SEVERITY IN ORGANOPHOSPHORUS POISONING CASES

GURVINDER SINGH	RESIDENT, DEPARTMENT OF MEDICINE, DR SN MEDICAL COLLEGE, JODHPUR.
INDU THANVI	ASSOCIATE PROFESSOR, DEPARTMENT OF MEDICINE, DR SN MEDICAL COLLEGE, JODHPUR.
SHYAM MATHUR	SENIOR PROFESSOR, DEPARTMENT OF MEDICINE, DR SN MEDICAL COLLEGE, JODHPUR.
NAMIT MATHUR	SENIOR RESIDENT, DEPARTMENT OF MEDICINE, DR SN MEDICAL COLLEGE, JODHPUR.
PURAN SAINI	RESIDENT, DEPARTMENT OF MEDICINE, DR SN MEDICAL COLLEGE, JODHPUR.
RAJAT TUTEJA	RESIDENT, DEPARTMENT OF MEDICINE, DR SN MEDICAL COLLEGE, JODHPUR.

ABSTRACT Organophosphorus compounds are commonly used insecticide poisons in India due to easy availability and use in agriculture. They reduce acetylcholinesterase levels in serum and RBCs. Serum levels of serum creatine kinase often elevates in Organophosphorus poisoning cases. This study was conducted to see the correlation of serum creatine kinase levels correlation with organophosphorus poisoning case severity and prognosis. 40 patients were selected with exposure to organophosphorus compounds and their serum creatine kinase levels were evaluated on day one prior to initiation of treatment and it was correlated with outcome of patients, total dose of atropine used in treatment and duration of stay in hospital.

KEYWORDS :

INTRODUCTION

Organophosphorus (OP) compounds are one of the most common causes of insecticide poisoning worldwide. 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(1). According to an Indian study, the incidence of OP poisoning was around 1.26 lakhs during the period of 12 months in 2007, as reported by Ravi *et al(2)*. 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, isoflurophate), antihelmintics (such as trichlorfon), 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 symptoms like miosis, bradycardia, increased gastrointestinal motility, emesis, sweating, tachypnea, salivation, lacrimation, altered sensorium, fasciculation, bronchospasm, blurred vision, photophobia, urination and defecation. Complications include acidosis, respiratory paralysis, acute renal failure, seizures, arrythmias, aspiration, coma and even death. The causes of death in OP poisoning may be either one or a combination of the above. Early diagnosis is a key to cure. A delay of initiation of treatments limits not only outcome, but also the opportunity to use 2-PAM (cholinesterase re-activator) which prevents "aging" of the enzyme. Till now, investigations comprised serum 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, 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(3). There are emerging options for new cheaper and/or easily quantifiable biochemical markers in relation to OP poisoning like creatine phosphokinase (CPK), lactate dehydrogenase (LDH), serum immunoglobulins (IgG, IgA), circulating complements (C3, C4), etc(4). But immunoglobulin assays, apart from being costly and difficult to perform in most laboratories, are often unreliable. Several animal model studies on rat liver and fresh-water snails indicate the association between OP poisoning and CPK levels(5). In a study, it was proposed that serum level of CPK is often found to be elevated in OP poisoning and may be used as a biomarker(5).

With this background in mind, we undertook a study to assess the role of CPK as an alternative prognostic marker and to establish a correlation between CPK levels and the severity of OP poisoning.

MATERIAL & METHODS

The present study was conducted in Department of Medicine at MDM Hospital attatched to Dr.S.N. Medical college,jodhpur.Participants if conscious or their close relatives if patients were altered after understanding the study protocol and procedure was asked to give their written consent for the study. 40 patients were studied who consumed organophosphorus compound. It was a prospective study and period of study was from 1 june,2016 to 31 december,2016.The diagnosis of organophosphorus poisoning was based on history given by attendants,clinical signs and symptoms and poison brought by attendants and relatives.Patients with indication of exposure to a entirely different poison other than OP Poison,OP poisoning and mixed with any other poison, consumed poison along with alcohol,Patients of acute myocardial infarction or myocarditis,chronic alcoholic, with history suggestive of chronic liver disease,history suggestive of myopathy,history of malignancy and autoimmune diseases, history of renal disease, exposure to statins,fibrates, dexamethasone.Sample was collected aseptically by a single prick after initial resuscitation, from a peripheral vein without tying any tourniquet. The levels of serum CPK were measured following admission. During the course of treatment, I/M injections were avoided. They were treated with 2-PAM (adult dose is 1-2 g intravenously followed by 0.5 g/hour infusion) and initial dose of injection atropine 2 mg followed by infusion until the signs of "atropinization" occurred, i.e., heart rate>90/min and dilatation of initially constricted pupil. The total dose of atropine (mg) until the final clinical outcome (complete recovery or death) was calculated for each patient. The normal value of serum creatine kinase was taken 49-289 IU/L for males and 42-281 IU/L for females.

RESULTS

40 patients were enrolled in study out of which 25 were males and 15 females.27 patients were from rural background and 13 patients were from urban background,predominantly from lower and middle socioeconomic status according to Modified Kuppuswamy scale.Most

of them were students,others were farmers,labourers and housewives.Commonest OP compound consumed in our study was found to be chlorpyrifos 20%,in 23 patients out of 40(57.5%),which is agricultural pesticide.

TABLE1 : Age distribution with sex

Age (yrs)	Male	Female	Total
0-15	2	2	4
16-30	17	11	28
31-45	5	2	7
46-60	1	0	1

Table 1 shows age and sex distribution of OPC poisoning cases.

Graph 1 showing age distribution of subjects with sex

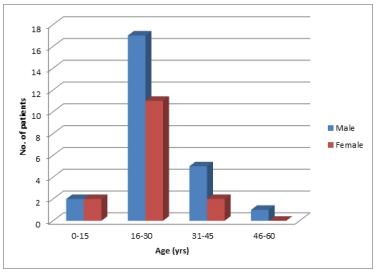


Table 2: Correlation of Creatine kinase level with patient outcome

Patient outcome	No. of patients	Creatine kinase level (IU/L)(Mean±SD)	P value
Survived	32	421.57±359.40	<0.0001 (HS)
Expired	8	1739.93±467.10	

Table 2 shows the correlation of creatine kinase with patient outcome. Out of 40 subjects 32 survived and 8 expired. Mean creatine kinase levels in survived subjects was 421. 57 and in expired patients was 1739.93(p value<0.0001).

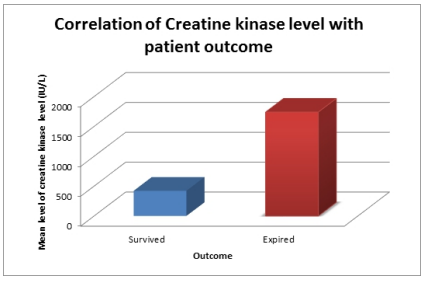


Table 3 : showing creatine kinase levels correlation with patients admitted in ICU

Intubated or not	No. of patients	Creatine kinase level (IU/L) (Mean±SD)	p value
Yes	14	1437.68±507.83	0.002
No	5	608.5±93.12	

Table 3 shows correlation of creatine kinase levels with patients admitted in icu. Out of 40 patients 19 were admitted in icu. Out of 19 icu patients 14 wew intubated and 5 were non intubated. Mean creatine kinase levels were 1437.68 IU/L in intubated patients and in non intubated were 608.5 IU/L (p value<0.005).

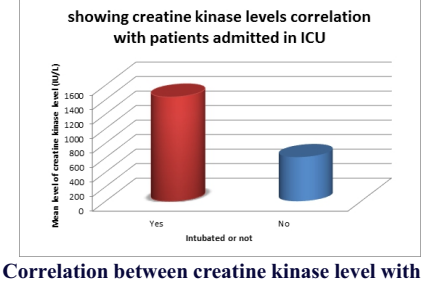


Table 4: Correlation between creatine kinase level with total dose of atropine in survived patients

	Creatine kinase level(IU/L)	Total atropine (mg)	r value
(Mean±SD)	421.57±359.40	109.5±47.78	0.94

Table 4correlation between creatine kinase with total dose of atropine dose in survived patients. Mean creatine kinase levels in survived patients were 421.57 IU/L and mean atropine dose given was 109.5 mg.® value=0.94).

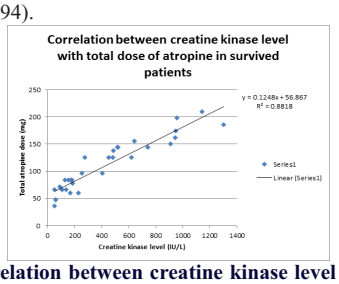
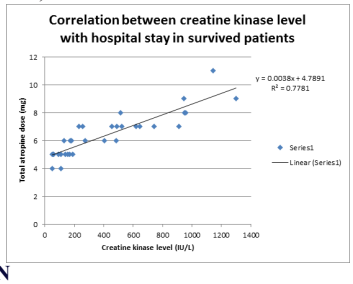


Table 5: Correlation between creatine kinase level with hospital stay in survived patients

	Creatine kinase level(IU/L)	Hospital stay (days)	r value
(Mean±SD)	421.57±359.40	6.40±1.56	0.88

Table 5 shows correlation between creatine kinase levels with hospital stay in survived patients. Mean creatine kinase levels were 421.57 IU/L in survive patients and mean duration of hospital stay was 6.4 days.® value=0.88).



DISCUSSION

The present study was a hospital based observational cross sectional study in WESTERN RAJASTHAN assessing serum levels of creatine phosphokinase as prognostic marker in organophosphorus poisoning cases. We determined serum CK levels at time of admission.

The socio-demographic features of study subjects were according to the patients admitted with organophosphorus compound poisoning in MDM Hospital,Jodhpur. The number of subjects studied were 40,out of these 25(62.5%) were males and 15(37.5%) were females. There were higher number of rural subjects in this study 27(67.5%) in comparison to urban subjects 13(32.5%).

Our study showed that patients with higher levels of serum CK levels expired as compared to low levels. Patients with higher CK levels got admitted initially in ICU and total duration of stay was longer in patients with higher levels of serum CK. Total dose of atropine needed was also higher in patients with high serum CK levels.

Most of subjects were in age group 16-30 yrs.(28 out of 40). Subjects in age group 0-15 yrs were 4, in age group 31-45 yrs were 7 and in age group was 1. Out of 40 patients 32 survived and 8 expired. Mean creatine kinase levels in survived patients were 421.57 IU/L and in expired patients were 1739.93 IU/L. Out of 40 patients 21 were admitted in ward and 19 were admitted in icu. Out of 19 patients admitted in icu 14 were intubated and 5 were non intubated. Mean creatine kinase levels in intubated patients were 1437.68 IU/L and in non intubated patients were 608.5 IU/L.

Serum CK levels were high in patients who expired, needed prolonged stay, required more atropine or were intubated. Serum CPK level might be helpful in predicting as well as assessing the prognosis of patients of OP poisoning.

CONCLUSION

Serum CPK level can be used as biomarker in case of acute OP poisoning due to its easy availability, cost effectiveness,. However, the main disadvantage with this marker is its non-specificity. Other causes of raised serum creatine kinase levels has to be excluded. Further studies with greater number of patients are required to support our observation, since our study was conducted with a relatively small number of patients, and in only one center located in western India, which might prejudice any comment on its efficacy and reliability among other ethnic groups.

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