Original Paper

Isoenzyme Pattern of Creatine Kinase in Acute Organophosphorus Compound Poisoning

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ABSTRACT

Pesticide poisoning is an important cause of mobidity and mortality in many developing countries. Many organophosphorus (OP) pesticide poisoning cases are reported in teaching medical college hospitals of Tamil Nadu every year. Generally, routine biochemical parameters are studied in detail in acute OP poisoning cases. In this study, an attempt was made to study the isoenzyme pattern of serum creatine kinase (CK) in acute OP poisoning. Acute OP cases were classified according to severity of poisoning. Eight cases in each grade (1, 2, 3 & 4) were selected for the study from IMCU and Toxicology ward of Government General Hospital, Chennai between August 2005 and April 2008, and analysed for isoenzyme of CK. Results revealed elevation of 100% CK-MM fraction of CK for Grade 1, 2 & 3 acute OP poisoning cases. Grade 4 cases showed a mild increase in CK-BB and CK-MB fractions along with predominant CK-MM fraction. The increase of CK in acute OP cases is primarily due to respiratory or pulmonary disorder and is not derived from cardiac or skeletal muscles of the body.

Key Words: Creatine kinase; Adenosine triphosphate; Organophosphorus compound; Myocardium

Introduction

Pesticide poisoning is an important cause of morbidity and mortality in many countries. It has been estimated that 3 million cases of severe poisoning and 2,20,000 deaths occur every year in the world, of which 99% occur in developing countries, particularly among farm workers.[1,2] Organophosphorus (OP) and carbamate compounds are the insecticides most commonly used worldwide in the pest control of crops. Because of their easy availability and accessibility they have been commonly used for suicidal purposes in developing countries over decades. OP pesticides have gained more popularity worldwide compared to organochloride (OC) compounds, which are persistent and highly damaging to the environment.[3]

Various biochemical parameters have been studied in detail in acute OP cases. We have focused on a specific enzyme, namely creatine kinase (CK) which was found to be elevated in many acute OP cases. Increase of CK enzyme in acute OP cases have also been reported earlier in humans.[4] The objective of our study was to find out the isoenzyme pattern of CK in acute OP cases, and to assess the maximum tissue damage or organ damage.

Creatine kinase (CK) is involved in energy storage in tissues, primarily muscle. During active muscle contraction, adenosine triphosphate (ATP) is used up and creatine phosphate is converted by CK to creatine and ATP. For continuous contraction, during periods of rest, ATP is converted to creatine phosphate by CK to serve as an energy reservoir. CK is predominantly found as a dimer of catalytic subunits, each with molecular weight of about 40 kDa; the two sub units are termed M (for muscle) and B (for brain). The three resulting isoenzymes are CK_1 (BB), CK_2 (MB) and CK_3 (MM).

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Materials and Methods

Acute OP cases were graded according to the method of Ballantyne and Marrs.[5]

Gr. 1 - No signs and symptoms
Gr. 2 - Symptoms such as diarrhoea, abdominal pain and giddiness
Gr. 3 - Pupillary constriction, with or without the symptoms mentioned above.
Gr. 4 - Pulmonary oedema, with or without the findings of Gr. 2 & Gr. 3.
Gr. 5 - Unconscious, with components of Gr. 2 to Gr. 4

Eight cases in each grade (1, 2, 3 & 4) were selected for study from the IMCU and Toxicology ward of Govt. General Hospital, Chennai between Aug 2005 and April 2008. Informed consent was obtained from the attendees of the patients. The study was approved by the Ethics Committee of Madras Medical College, Chennai. Acute OP grade 5 cases were admitted in unconscious state and required ventilatory support; hence they were not included in the study. Blood samples were collected on admission and were analysed for total CK and isoenzymes of CK.

Analysis Of Total CK: Total CK was analysed by semi auto-analyser (microlab 200) by UV kinetic IFCC method. CK catalyzes the conversion of creatine phosphate and ADP to creatine and ATP. The ATP produced reacts with glucose and gets converted to ADP and glucose-6-phosphate by hexokinase (HK) in the second reaction. In the final reaction, glucose-6-phosphate dehydrotgenase (G-6-PD) oxidizes the glucose-6-phosphate produced in the second reaction and reduces NADP. The NADPH produced in the final reaction is proportional to the creatine produced in the initial reaction. The rate of increase in NADPH absorption at 340 nm is thus directly proportional to the CK activity. The total CK activity is expressed in U/L at 37°C.

Results and Discussion

Total CK was moderately elevated (**Table 1**). Our results pertaining to CK isoenzyme showed elevation of 100% CK-MM fraction for all Grade I, II & III acute OP cases. Group IV OP cases showed a mild elevation of CK-BB and CK-MB fractions (**Fig**). CK-MM is mostly present in skeletal muscle. If the cardiac muscle had been damaged , CK-MB would be raised. In our study, we noticed increase of CK-MB only in Gr.IV cases, along with elevated CK-BB fraction.

In the normal heart, an average of 15% to 20% of the CK is CK-MB. Its distribution is not uniform, with CK-MB percentage greater in the right heart than in the left heart.[6] A single study however suggests that CK-MB is not found in normal myocardium.[7]

In Grade I, II, III cases we observed only CK-MM muscle fraction (**Fig**) indicating the damage of skeletal muscle of limbs, and respiratory and lung tissues. As there was only 2 to 3 fold increase of total CK, we assumed that the CK isoenzymes release may be primarily from lung or respiratory skeletal muscle. If skeletal muscles of limbs were involved, we would observe manifold increase in total CPK as seen in persons doing exercise. Exercise is a major variable in CK-levels. There is a direct relationship between intensity of exercise in men and CK, particularly with strength exercise.[8] Also, during regeneration of skeletal muscle, increased amounts of CK-MB are produced relative to CK-MM, similar to the pattern seen in total muscle.[9] Respiratory muscles contain more CK-MB than most muscles (3 to 7%). An increased percentage of CK-MB is often seen in those with acute respiratory exertion due to lung disease exacerbation. Also, increased use of respiratory muscle in those with obstructive lung diseases can cause elevation of CK.[10] In our study, we observed an increase of CK-MB (6.2%) and CK-BB (8.1%) in Gr.IV (**Fig**), and increase of CK-MM fractions in Gr.I, II & III cases (**Fig**), indicating the involvement of respiratory and pulmonary disorders. Also, since acute OP patients exhibit signs and symptoms of respiratory and pulmonary disorders, we suggest that the increase in CPK may be due to respiratory and pulmonary disorders, and not from cardiac or skeletal muscles of the body.

Table 1 Results of Creatine Kinase (CK) (in microlitre)

Sl. No	Gr.I	Gr.II	Gr.III	Gr.IV
1.	396	384	712	510
2.	284	310	480	664
3.	405	426	624	526
4.	494	426	510	440
5.	505	584	426	382
6.	356	610	312	294
7.	410	436	605	344
8.	477	296	595	308

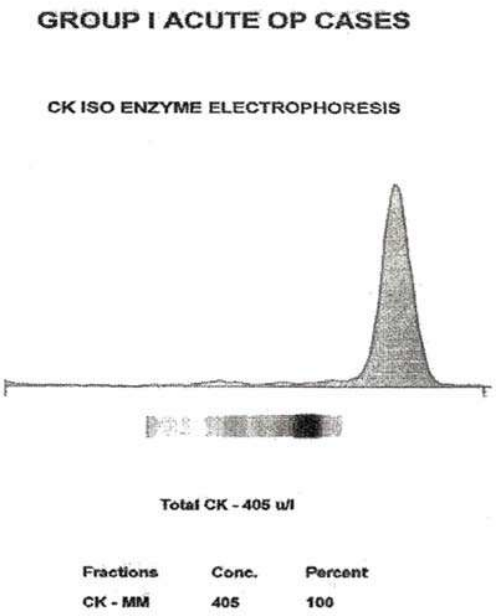

Fig 1.

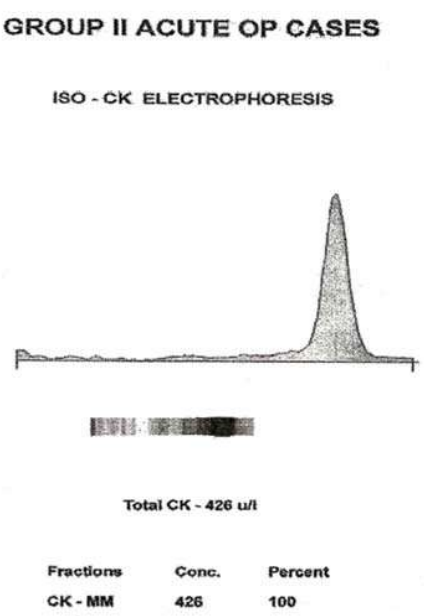

Fig. 2

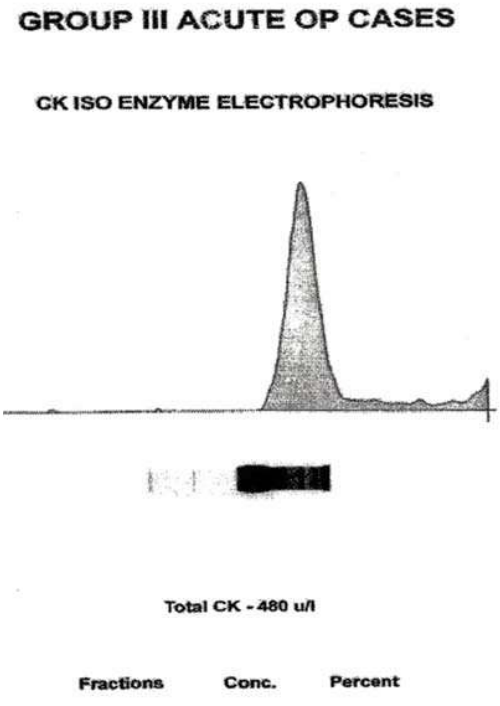

Fig 3.

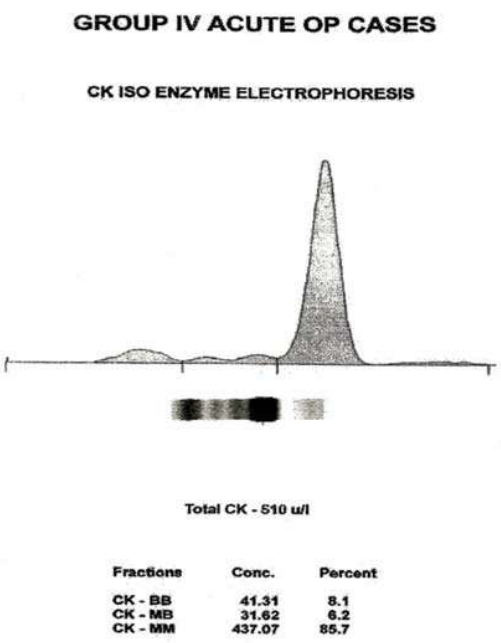

Fig. 4

Conclusion

The increase of creatine kinase (CK) in acute organophosphorus (OP) poisoning cases are primarily due to respiratory or pulmonary dysfunction, and not derived from cardiac or skeletal muscles of the body.

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