



SERUM CREATINE KINASE AND MAGNESIUM AS PROGNOSTIC INDICATORS IN OP COMPOUND POISONING

Dr.Sudhakar P

Professor of Medicine, Kurnool Medical College, Kurnool.

Dr.Blessy Manohar. V*

Assistant Professor of Medicine, Kurnool Medical College *Corresponding Author

Dr.Nikhitha K

Senior Resident in Medicine, Kurnool Medical College, Kurnool.

ABSTRACT Agriculture constitutes the major component of Indian economy. Pesticides are wonderful human inventions used for the control of pests, weeds or plant diseases to improve the cultivation of agricultural products. It also had been used as chemical warfare weapons. Organophosphorus (OP), the commonest agent for poisoning in India due to its easy availability, acts by inhibiting acetylcholinesterase at muscarinic and nicotinic receptors. Erythrocyte cholinesterase (EchE) and plasma cholinesterase (PchE) are reduced in OP poisoning, but their estimation is costly and not regularly performed. There are emerging options for new cheaper biochemical markers in relation to OP poisoning. Serum level of creatine phosphokinase (CPK) is often found to be elevated and serum magnesium is often reduced in OP poisoning. This study was conducted to see if CPK and magnesium may be used as an alternative of cholinesterase levels in blood to assess the severity of OP poisoning. This was a prospective and observational study. Sixty patients of OP poisoning without any prior treatment, presenting within 12 hours, were selected and their clinical severity was categorized according to Peradeniya organophosphorus poisoning (POP) scale. Level of serum CPK, blood EchE and serum Mg were measured following admission, and total dose of atropine (mg) until the final clinical outcome (complete recovery or death) was calculated. Our study recommends serum CPK and Magnesium as alternative markers

KEYWORDS : Acetylcholinesterase level, creatine phosphokinase, organophosphorus poisoning, Peradeniya organophosphorus poisoning scale

INTRODUCTION:

In India, agriculture is still labour-intensive. So, man is exposed to such chemicals at all stages of pesticide formulation, manufacturing and spraying in his farm. Pesticides has got both acute and chronic health hazards upon exposure either by occupational or by self-harm (1).

Poisoning constitutes about 60% of self-harm(1) in rural Asia, Organophosphate compounds account for 80% of pesticide poisoning. Ravi et al described the incidence of organophosphorus poisoning as around 1.26 lakhs during the year 2007 in India. In our Govt. General Hospital, Kurnool 330 and 244 cases of acute organophosphorus poisoning admitted respectively in 2015 and 2016 with a mortality rate of 19% mostly due to respiratory paralysis and mechanical ventilation related complications.

Even with this background, the medical management of acute organophosphorus poisoning is deficient in evidence based management protocols and research tool. This calls for our urgent comprehensive analysis of acute organophosphorus poisoning which may be helpful in renovating the protocol in its management to reduce mortality.

AIMS & OBJECTIVES:

1. To assess and categorize the severity of organophosphorus poisoning cases clinically, on admission by Peradeniya Organophosphorus Poisoning scale.
2. To estimate and correlate the serum levels of creatine kinase and magnesium with the clinical severity scoring, with the atropine requirement during course in hospital, with one or more of complications like respiratory paralysis, intermediate syndrome and the need for mechanical ventilation, acute renal failure, seizures, arrhythmias and coma.

MATERIALS & METHODS:

Setting:

The study was conducted in the Department of General Medicine, Govt. General Hospital, Kurnool. It was a cross sectional prospective study done during the period from June 2015 to September 2016.

60 patients, admitted as a case of acute organophosphorus poisoning with exposure within 12 hours irrespective of route of exposure, age and sex were selected and subjected for study with the consent.

Exclusion Criteria:

1. Patients with other pesticide poisoning (e.g. organocarbamates) have been excluded by history and clinical features
2. Patients with mixed poisoning were excluded.
3. Patients who had taken compounds with alcohol have been excluded.
4. Patients with known medical illness such as chronic liver disease, myopathy, malignancy, renal failure, autoimmune diseases, seizure order, coronary artery disease were excluded.
5. Patients who were on chronic drug usage with statins, steroids, diuretics have been excluded
6. Pregnant patients were excluded from the study.

The eligible patients were assessed clinically on admission by Peradeniya Organophosphorus Poisoning scales and categorized according to the severity. They were subjected to routine blood investigations like blood sugar, blood urea, serum creatinine, liver function test, serum acetylcholinesterase, ECG and ABG. They also have been subjected to estimation of serum creatine kinase and magnesium levels on admission.

Bio chemical markers and the methods employed

1. Cholinesterase: Kinetic Calorimetric method
2. Creatine Kinase: NAC activated method (kinetic)
3. Magnesium: Chlorophosphonazo III

First, the clinical severity by POP scoring were correlated with initial serum creatine kinase and magnesium levels.

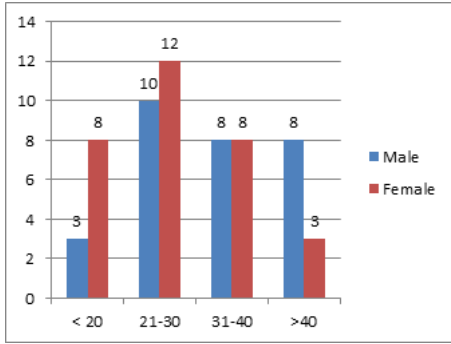
Statistical methods

Statistical analysis was done using SPSS software. The following statistical methods have been employed for analysis:

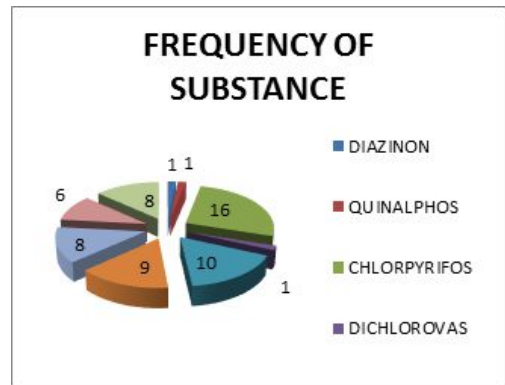
1. Chi-square test
2. Unpaired student test
3. Analysis of variance (ANOVA)

RESULTS

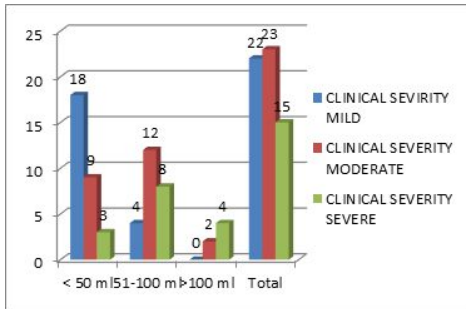
In our series, among 60 patients taken for study. 37% constitutes the age group between 21-30 years. The number of people between the age group 21-40 accounts for 38 out of 60 cases. Which forms the majority Female population predominates with 52%.



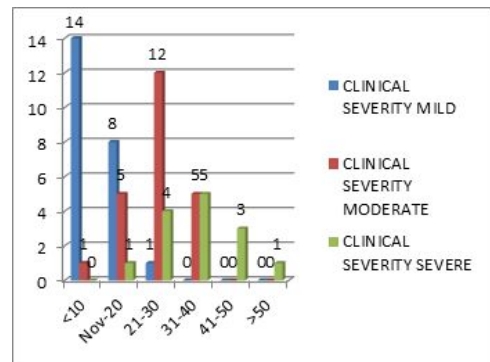
FREQUENCY OF SUBSTANCE EXPOSED



QUANTUM OF EXPOSURE AND CLINICAL SEVERITY BY POPSCORING

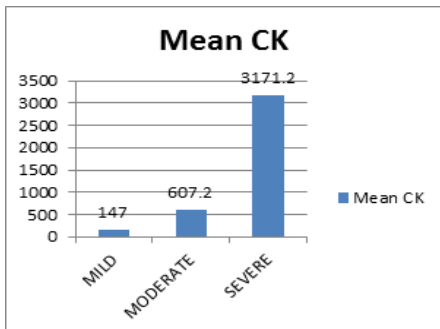


ATROPINE DOSE REQUIREMENT AND CLINICAL SEVERITY



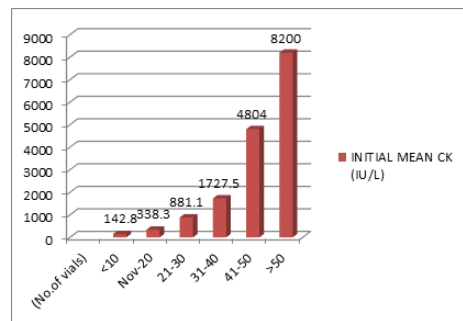
CLINICAL SEVERITY AND INITIAL MEAN SERUM CK VALUES

The clinical severity positively correlates with the initial mean serum creatine kinase levels ($p < 0.001$). Thus, the severe poisoning cases will have high serum creatine kinase levels at admission and mild poisoning have normal levels while moderate cases lie in between and is significant. This elevation of serum creatine kinase is due to the muscle fiber necrosis produced due to the high toxicity of the OPC compounds.



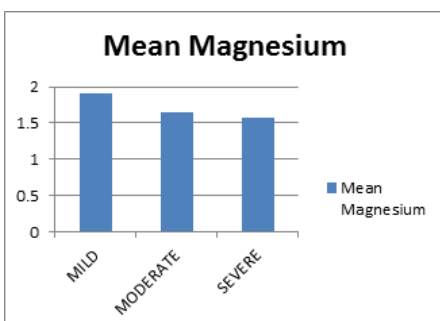
ATROPINE DOSE REQUIREMENT AND INITIAL MEAN CK LEVELS

The comparison of atropine dose requirement and initial mean serum creatine kinase is significant with the positive correlation ($p < 0.001$).



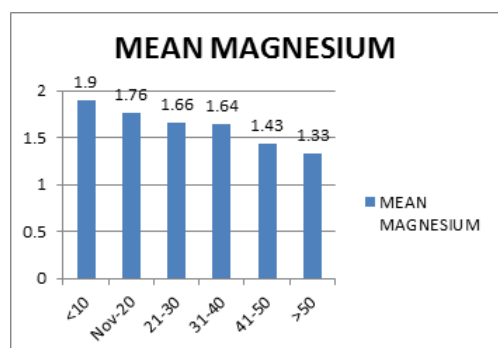
CLINICAL SEVERITY AND INITIAL MEAN MAGNESIUM VALUES

As severity of organophosphorus poisoning is associated with the reducing levels of serum magnesium, it has negative correlation ($p < 0.001$).



ATROPINE DOSE REQUIREMENT AND INITIAL MEAN MAGNESIUM LEVELS

The comparison of atropine dose requirement and initial mean serum magnesium level is significant with the negative correlation ($p < 0.001$) i.e. patients with low serum magnesium level at admission will require large doses of atropine.



DISCUSSION:

In this series, the organophosphorus poisoning was most prevalent in the age group 21-30 years. 49 cases out of 60 were below the age of 40 years. Pyar Ali et al observed the mean age group of 28.6±9.8 years from Karachi. Another study from Karachi by AftabTurab et al observed the age group of 15-20 years (44.74%) as predominant. Murat Sungur et al from Turkey observed the mean age group as 30±15 years. Karallidde L., Senanayake N. et al¹ of Srilanka documented 91% of their cases were under the age of 30. Malik et al from Kashmir, revealed the predominant population affected by OPC exposure were under the age of 25. In Mangalore, Karnataka, India, the most common age group to be affected was between 20-30 (36.6%). KuntalBhattacharya et al of Kolkata reported the mean age of 25.5 years. This young age group affected by exposure and also in terms of procurement and productivity. This study throw light on the target age group by improving the management protocol and decreasing the mortality.

In our series, females (n+31) dominated the study population. Probably many male patients were excluded from study due to the mixed poison with alcohol. Malik et al observation of 122 cases in Kashmir valley (females n+114, males n+50), female intoxication was more. In mangalore and Srilanka had pattern to the case series with male predominance. S. Shivakumar and K. Raghavan et al of Tamilnadu reported 165 cases of organophosphorus poisoning and sex distribution was with male predominance. KuntalBhattacharya et al from Kolkata showed male predominance. In southern part of India, males are actively involved in spraying fertilizers and pesticides.

In our case series, 23 out of 60 (38.3%) were agriculturists. Non agriculturist were exposed more to organophosphorus compounds with the suicidal intent. In Agriculturist also accidentally exposed due to the spraying in the field. In Kashmir Valley, two third of the population who had exposed were engaged in apple orchard.

In our series, most of the cases occurred due to ingestion (98.3%) and only one had accidental inhalation (1.7%). The common organophosphorus compounds abused in our series are chlorpyrifos and imethoate. KuntalBhattacharya et al also described the most frequent compound as Chlorpyrifos (38.1%).

Clinical severity by Peredeniva Organophosphorus Poisoning scale

Kuntal Bhattacharyya et al of Kolkata correlated initial serum creatine kinase with the clinical severity by POP scoring and outcome. In our study, POP scoring was much reliable that it correlated clearly with the duration of hospital stay, development of complications, quantum of exposure and initial serum creatine kinase, magnesium values.

Laboratory correlates: Serum Magnesium

Hypomagnesemia seems to occur in any critical illness patients according to various studies. Hypomagnesemia in acute organophosphorus poisoning cases might be due to GI losses, vomiting, diarrhoea, prolonged gastric aspiration, etc., magnesium is one of the omitted electrolyte in any illness. Since, many manifestations of hypomagnesemia overlap with features of organophosphorus poisoning, it may be the contributory factor in severity and outcome.

In our study, decreased serum magnesium levels at admission correlated with poor outcome in the form of increased atropine requirement, duration of hospital stay, Incidence of intermediate syndrome, mechanical ventilation, death and not correlated with the incidence of renal failure, seizures and arrhythmias.^{2,3}

There are studies regarding the beneficial effects of intravenous magnesium sulfate in the management protocol of organophosphorus poisoning. The mechanism for magnesium sulfate is blocking of ligand gated calcium channels, resulting in reduced acetylcholine release from pre-synaptic terminals.

Hence, it is our opinion from the study that initial reduced serum magnesium level will correlate with poor clinical outcome and intravenous magnesium sulfate also corrects hypomagnesemia in

addition to the reduction in acetylcholine release from pre synaptic terminals.

Laboratory correlates: Serum Creatine Kinase

Patients with acute organophosphorus poisoning are usually monitored by using serum acetylcholinesterase levels which are expected to fall. But, this investigation can not be available in every hospital is also expensive. Hence, we preferred the estimation of serum creatine kinase instead, which is cheaper.

The initial rise of serum creatine kinase in severe acute organophosphorus poisoning is probably due to the presence of muscle fiber necrosis. This has been demonstrated in two patients by Kuntal Bhattacharyya et al⁷ This occurred even before the development of intermediate syndrome in which CK level is expected to rise. The mean half life of CK is about 1.5 days. With the good management, CK levels may be reduced to normal within 5 days if patient does not develop intermediate syndrome.

In our study, raised serum CK levels at admission significantly correlated with the initial clinical severity by POP scoring, increased atropine requirement, duration of hospital stay. It also correlated with the incidence of intermediate syndrome, arrhythmias, renal failure, coma, outcome. Thus, with serum cholinesterase levels at admission. Hence, we concluded that initial serum creatine kinase can be used as parameter for assessing the severity and outcome of acute organophosphorus poisoning replacing serum acetylcholinesterase levels from presynaptic terminals, thus reducing morbidity and mortality.

CONCLUSION:

1. Organophosphate poisoning is more prevalent among 21-30 years age group in our study which is in concordance with other studies but it is differing with other studies in having females as predominant category.
2. In our study patients admitted as severe poisoning required large doses of atropine. Hence we conclude that the clinical severity is estimated from POP score is worth taking to correlate with the laboratory parameters and outcome in acute organophosphorus poisoning.
3. Serum creatine kinase can be an efficient biomarker as predictor of severity of acute organophosphorus poisoning and be used instead of serum acetylcholinesterase levels considering the cost and non-availability.
4. Serum magnesium can be used as the predictor of severity of acute organophosphorus poisoning and intravenous magnesium sulfate to be considered for correlation to reduce the morbidity and mortality.

SUMMARY:

Organophosphorus poisoning is a menace to the human race both as a weapon of mass destruction and a misused pesticide of self-harm. Organophosphate compounds account for 80% of pesticide poisoning. The case fatality rate exceeded 60% in developing countries where there are many pitfalls in treatment protocol and research activities. Hence, we conducted a study with 60 patients for the possible role of serum creatine kinase and magnesium at poison centre,

We found that, raised serum creatine kinase and reduced serum magnesium levels in acute organophosphorus poisoning at admission indicates poor outcome and emphasized the future research regarding the beneficial effect of intermediate magnesium sulfate for correcting hypomagnesemia to reduce the morbidity and mortality.

REFERENCES:

1. Michael Eddleston, M H Rezvi Sheriff, and Keith Hawton. Deliberate self harm in Sri Lanka: an overlooked tragedy in the developing world. *BMJ* 1998 July 11;317 (7151): 133-135.
2. Petroianu GA. The synthesis of phosphor ethers: who was Franz Anton Voegeli? *Pharmazie* 2009 Apr; 64 (4): 269-75.
3. Seigfried Franke. *Manual of Military Chemistry: Chemistry of chemical warfare agents.* (Volume 1)
4. H.J. de Silva, R. Wijewickrema, N.Senanayake. Does pralidoxime affect outcome of management in acute organophosphorus poisoning? *Lancet* 1992; 339 (8802): 1136-1138.
5. Liska D, Kolesar D. Toxicological classification of pesticides. *Czech Med* 1982; 5(3):

- 137-45.
6. R.S.Wadia, C.Sadagopan, R.B.Amin, and H.V.Sardesai. Neurological manifestations of organophosphorus insecticide poisoning. *J NeurolNeurosurg Psychiatry* 1974 July; 37(7): 841-847.
 7. Kuntal Bhattacharyya, SibajiPhaujdar, Rathindranath Sarkar, and Omar S. Mullick. Serum Creatine Phosphokinase: A Probable Marker of Severity in organophosphorus poisoning. *Toxicollnt* 2011 Jul-Dec; 18(2)
 8. H.J. de Silva, R. Wijewickrema, N.Senanayake. Does pralidoxime affect outcome of management in acute organophosphorus poisoning? *Lancet* 1992; 339 (8802): 1136-1138.