IJPRP

Indian Journal of Pathology: Research and Practice

Volume 7 Number 2, February 2018
DOI: http://dx.doi.org/10.21088/ijprp.2278.148X.7218.11

Original Research Article

Hematological Profile in Acute Organophosphorous Compound Poisoning

Thinakaran Vijitha[a], Nirmala Mysore Jayakumar[b], Udaya Kumar Manikyam[c], Rudrappa Prashanth[d]

[a]Junior Resident [b]Associate Professor [c]Professor & Head [d]Assistant Professor, Department of Pathology, P.E.S. Institute of Medical Sciences and Research, Kuppam, Andhra Pradesh 517425, India.

Abstract

Context: Organophosphorus (OP) compounds are the most common suicidal poisons in the developing countries. A recent study from south India reported mortality rate of 4% in OP poisoning cases.These compounds exert their toxicity by allowing acetylcholine to overact at its receptors in the central and peripheral nervous system.

Aims: The aim was to study the variations in the hematological parameters in patients of OP compound poisoning and clinically correlate these findings with the severity of poisoning and assess the effect of treatment on them.

Methods and Material: Patients with definite history of OP compound poisoning and decreased serum levels of pseudocholinesterase (PCE) enzyme were included in the study. The serum pseudocholinesterase levels were estimated at admission. Another EDTA blood sample was subjected to complete blood picture analysis. The same methodology was repeated after treatment. OP poisoning patients were classified into latent, mild, moderate and severe based on serum pseudocholinesterase levels. Concurrently the changes in hematological parameters were correlated with the severity of poisoning before and after treatment.

Statistical Analysis Used: Statistical analysis of the percentages, mean, range and chi-square test for associations and Wilcoxon signed-rank test to assess the association were done, with p-value of <0.05 taken as statistical significance at 95% confidence interval

Results: The present study showed significant decrease ($p<0.001$) in serum cholinesterase levels in moderate to severe poisoning. Out of 164 cases, 80 of them showed neutrophilia at admission and reached to values of normal reference range in 81.2% of the cases post-treatment while neutophilia persisted in 18.8% despite treatment which is statistically significant.

Conclusions: This study concludes that in resource poor settings where estimation of plasma ChE levels cannot be determined then hematological parameters like total and differential leucocyte counts can predict response to treatment and recovery from OP poisoning.

Keywords: Organophosphorus Compounds; Poisoning; Serum Pseudocholinesterase; Neutrophilia.

Corresponding Author:

Nirmala Mysore Jayakumar, Associate Professor, Department of Pathology, P.E.S. Institute of Medical Sciences and Research, Kuppam, Andhra Pradesh 517425, India.
E-mail: nirmalamj60@gmail.com

(Received on 14.01.2017, **Accepted on** 09.02.2018)

Introduction

Organophosphorus (OP) compound poisoning is a major health problem not only in developing countries but also in developed countries [1]. Hospital based statistics suggest that nearly half of the admissions to emergency

with acute poisoning are due to OP compound poisoning, with affliction of approximately 3 million population with 2,00,000 deaths annually, most of these occur in developing countries [2,3]. OP compounds are easily available across the counter as insecticides and nearly 90% of the poisoning are suicidal with a fatality rate of >10% [4]. The mechanism of action of organophosphate pesticide is by inhibition of two enzymes, one, carboxyl ester hydrolases and the other butyryl cholinesterase. Acetyl cholinesterase, an enzyme found on blood cell membranes that degrades the neurotransmitter acetylcholine (ACh) into choline and acetic acid. ACh is found in the central and peripheral nervous system, neuromuscular junctions and red blood cells. Butyryl cholinesterase (BChE), also called serum cholinesterase or pseudocholinesterase is a serine hydrolase that catalyzes the hydrolysis of esters of choline. It is a liver acute phase protein, inhibited by OP compounds in a similar way to AChE, but the specificity of the two enzymes are different. The leading cause of death in OP poisoning is respiratory failure. The mortality rate depends on the type of compound used, quantum ingested, general health of the patient and delay in diagnosis or treatment [4]. Oxidative stress results when pro-oxidants are insufficiently balanced by antioxidants, resulting in cellular damage [5]. One of the molecular mechanisms of the toxicity of the pesticides seems to be lipid peroxidation, as a consequence these compounds can disturb the biochemical and physiological functions of blood cells, hence the study was planned to assess the hematological parameters in acute OP poisoning.

Subjects and Methods

This study was undertaken from August 2014 to July 2016 at a tertiary care institution. Patients with definite history of OP compound poisoning and decreased serum levels of pseudocholinesterase (PCE) enzyme were included in the study. Under aseptic precautions, venous blood sample was collected in gel vacutainers prior to the initiation of treatment and subjected to estimation of serum pseudocholinesterase using Vitros 250.

Another blood sample collected in EDTA vacutainer was subjected to complete blood picture analysis using Sysmex XS-1000i automated hematology analyzer. The same methodology was repeated after treatment. Out of 164 cases, PCE levels were estimated in 151 cases before treatment and 150 cases after treatment. In 13 cases the PCE levels were not done due to poor socio-ecnomic status. OP poisoning patients were classified into latent, mild, moderate and severe based on serum pseudocholinesterase levels (Table 1). Concurrently the changes in hematological parameters were correlated with the severity of poisoning before and after treatment.

Statistical analysis of the percentages, mean, range and chi-square test for associations and Wilcoxon signed-rank test to assess the association were done, with p-value of <0.05 taken as statistical significance at 95% confidence interval.

Results

The study consisted of 164 cases of suspected OP compound poisoning. The most vulnerable age group was between 21–30 years with male predominance.The male to female ratio was 1.5 : 1. The majority of the patients were agriculturists followed by house wives with phorate and chlorpyrifos being consumed on a larger basis. Suicide was the intention of OP poisoning in most of the patients. The common symptoms and the sign presented were nausea, vomiting and miosis respectively. In this study, 12.8% of the cases were in latent stage, 10.4% in the mild stage, 4.3% in the moderate stage and 29.3% in the severe stage of OP poisoning. The present study showed significant decrease (p<0.001) in serum cholinesterase levels in moderate to severe poisoning. Out of 164 cases, 80 of them showed neutrophilia at admission and reached to values of normal reference range in 65 (81.2%) cases post-treatment while neutophilia persisted in 15 (18.8%) cases which is statistically significant. The normalization of other WBC parameters were also noted and was significant. There was no significant variation among other hematological parameters viz. hemoglobin levels, HCT, MCV, MCH, MCHC and RDW values (Table 2,3).

Table 1: Stages of severity based on PCE levels

Stages	Before Treatment (no. of cases)	%	After Treatment (no. of cases)	%	P value[a]
Normal	58	35.4	62	37.8	
Latent	21	12.8	45	27.4	
Mild	17	10.4	25	15.4	<0.01*
Moderate	7	4.3	17	10.4	
Severe	48	29.3	1	0.6	
Total	151	92.1	150	91.5	

a. Chi square test
*Statistically significant

Table 2: Statistical significance in hematological parameters in OP poisoning patients

Parameter	Mean Before Treatment	Mean After Treatment	Before Treatment / After Treatment P-value*	Statistical significance
Hematocrit	41.419	41.443	0.503	Not Significant
Hemoglobin	13.841	13.846	0.888	Not Significant
Red Blood Cell count	4.743	4.750	0.305	Not Significant
MCV	86.749	87.003	1.000	Not Significant
MCH	29.148	29.148	1.000	Not Significant
MCHC	33.37	33.37	1.000	Not Significant
RDW-CV	13.47	13.43	0.854	Not Significant
Platelet count	294.27	300.78	0.814	Not Significant
Total WBC count	12.058	10.204	<0.01	Significant
Neutrophils	71.58	59.105	<0.01	Significant
Lymphocytes	20.588	24.767	<0.01	Significant
Monocytes	5.729	4.361	<0.01	Significant
Eosinophils	1.928	1.746	0.799	Not Significant

Table 3: P values for Total White Blood Cell (WBC) count and Differential count

Total WBC Count	Neutrophils	Lymphocytes	Monocytes	Eosinophils	Basophils
<0.01*	<0.01*	<0.01*	<0.01*	.799	--

*Statistically Significance

Table 4: Comparision of Pseudocholinesterase mean values among other studies

Pseuducholinesterase level (IU/L)	Present Study	Panda et al	Chaudhary S et al
Mean	3976.94	3907.64	3154.16

Discussion

OP compound poisoning from intentional and accidental exposure is a major public health problem in the developing world [6]. Of various agents used for suicidal purposes in India, organophosphate and carbamate form a significant group in developing countries like India [7].

The present study showed significant decrease ($p<0.001$) in serum pseudo ChE levels (Table 4) and correlates with similar findings by Panda et al [8] and Chaudhary S et al [9]. The classic laboratory tests for OP toxicants are the inhibition of the serum pseudo ChE which is apparent within few minutes or hours of absorption of OP compounds. The clinical severity of organophosphorous poisoning is graded as mild, moderate, severe and fatal. In our study pseudo ChE values were significantly suppressed in moderate (4.3%) and severe (29.3%) poisoning cases, in comparison to patients with mild poisoning (10.4%). Similarly the P value was < 0.01 in a study conducted by Kang et al [10]. ChE activity correlated with the quantity of pesticides absorbed in the body and its inhibition also correlated with toxic manifestations in the body. However, recent reports have implied that the degree of serum ChE inhibition is considerably different in patients consuming different OP compounds. Therefore, it can be used to predict the need for emergency intervention when the organophosphate ingested is known and its diagnostic serum value has been studied [8]. The human body has several mechanisms to counteract with the damage produced by free radicals; the basic and the most prominent defense mechanisms are antioxidant agents that are present in serum.

Thus in acute OP poisoning sudden overproduction of reactive oxygen species leads to significant lipid peroxidation. The spurt in the utilization of non enzymatic anti oxidants and its non compensation in short time leads to lowered antioxidant acivity [5]. Ranjbar A et al reported significant lipid per oxidation accompanied with decreased total antioxidant activity and ChE activity [11].

The susceptibility of Leucocytes to oxidative stress due to pesticide exposure is a function of overall balance between degree of oxidative stress and antioxidant defense capability. Thus the OP compounds may directly or indirectly modify the antioxidant activity with consequent susceptibility to oxidative stress [12]. The study by Hundekari et al stated that cells continually suffer from oxidative stress despite antioxidant defense mechanisms like increased superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GPx) activity. The severity of OP poisoning is directly proportional to the stress and free radical generation. The free radical production is so high

that it overwhelms the elevated antioxidant activity failing to keep in check lipid peroxidation. The higher levels of antioxidant enzymes may be necessary to detoxify increased concentration of lipid peroxidation products [5].

In this study, the white blood cell count was significantly ($p< 0.001$) increased in all stages of OP poisoning . There was leucocytosis with neutrophilia in moderate and severe poisoning when compared to latent and mild poisoning. Increased sympathetic activity usually precipitates demargination, resulting in leucocytosis [13], consequently, it may be a prognostic marker in acute OP poisoning in association with intoxication. The alteration of leukocyte counts can be explained by the simultaneous occurrence of cholinergic stimulation along with an acute inflammation [10].

The results of this study showed no significant decrease in the mean value of hemoglobin before and after treatment in affected patients. This was against the finding by Hundekari et al who found (<0.05) significant decrease in hemoglobin and discussed it as a result of the decreased synthesis of hemoglobin. Another possible interpretation is binding of organophosphorous insecticides with iron, followed by a lack of incorporation of iron in hemoglobin leading to microcytic erythrocytes [5]. Further, there was no statistical significance in the values of hematocrit, MCV, MCH, MCHC, and RDW-CV.

Toxicities of OP compounds induce oxidative damage by elevating lipid peroxidase levels. Increased antioxidant enzymes may be attributed to adaptive response of erythrocytes to oxidative damage due to OP compounds. The significantly higher leucocyte count observed in the moderate and severe stages of OP poisoning implies the activation of the defense mechanism and immune system which could be a positive response for survival. This is confirmed in our study wherein the total leucocyte counts and differential leucocyte counts returned to normal reference range after treatment.

Conclusion

This study concludes that by estimating plasma ChE levels one can determine the severity of poisoning. But in resource poor settings the hematological parameters like total and differential leucocyte counts can predict response to treatment and recovery from OP poisoning.

References

1. Peter JV, Cherian AM. Organic Insecticides. Anaesth Intensive Care 2000;28:11-21.
2. Singh S, Sharma N. Neurological syndromes following organophosphate poisoning. Neurol India 2000;48: 308-13.
3. Fernando R. Pesticide poisoning in the Asia-Pacific Region and the role of a regional information network. J Toxicol Clin Toxicol 1995;33:677-82.
4. Selden BS., Curry SC. Prolonged succinyl choline-induced paralysis in organophosphate insecticide poisoning. Ann Emerg Med 1987;16:215-17.
5. Hundekari IA, Suryakar AN, Rathi DB. Acute organophosphorus pesticide poisoning in North Karnataka, India: oxidative damage, hemoglobin level and total leukocyte. African Health Sciences 2013;13:129-36.
6. Eddleston M, Karalliedde L, Buckley N, Fernando R, Hutchinson G, Isbister G, et al. Pesticide poisoning in the developing world—a minimum pesticides list. Lancet 2002;360:1163-67.
7. Singh S, Sharma BK, Wahi PL, Anand BS, Chugh KS. Spectrum of acute poisoning in adults (10 year experience). J Assoc Physicians India 1984;32:561-63.
8. Panda S, Mishra PK, Nanda R, Rao EV, Mangaraj M. Laboratory Abnormalities in Patients with Organophosphorus Poisoning. Indian Medical Gazette-2014;167:6-11.
9. Chaudhary S, Singh K, Sawlani KK, et al. Prognostic Significance of Estimation of Pseudocholinesterase Activity and Role of PralidoximTherapy in Organophosphorous Poisoning.Toxicology International 2013;20: 214-17.
10. Kang EJ, Seok S, Lee KH, Gil HW, et al. Factors determining survival in Acute Organophosphorus poisoning. KJIM 2009;24:362-66.
11. Ranjbar A, Solhi H, Mashayekhi FJ, Susanabdi A, Rezaie A et al. Oxidative stress in acute human poisoning with Organophosphorus insecticides: a case control study. Env Toxicol Pharmacol 2005;20:88-91.
12. Banerjee BD, Seth V, Bhattacharya A, Pasha ST, Chakraborty AK. Biochemical effects of some pesticides on lipid per oxidation and free radical scavengers. Toxicol Lett 1999;107:33-47.
13. Clark RF.Insecticides: Organic phosphorus compounds and carbamates.In: Goldfrank's Toxicologic Emergencies,7ed, The McGray-Hill companies,Inc. Chapter 88.p: 1346-57.