

Impairment in Clinical Indices in Acute Organophosphate Insecticide Poisoning Patients in India

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Abstract

This report defines with the impairment in clinical indices and laboratory investigations in acute organophosphate poisoning patients admitted to Outdoor Patient Department of B.J. Medical College and Civil Hospital, Ahmedabad – 380016, India. Out of 121 OP poisoning patients (65.3% males and 35.7% females), about 70% cases were educated (matriculate and higher secondary passed) and remaining illiterate. It was noticed that suicidal and intentional poisoning being a major cause as recorded in 80.2% cases followed by occupational (9.1%), accidental (6.6%), homicidal (1.6%) and unknown (2.5%).

The major signs and symptoms reported by the poisoning cases were muscarinic and nicotinic manifestations. ECG abnormalities were recorded in 46 cases (38%); the sinus tachycardia (24%), depression of ST segment and inversion of T wave (7.4%) and sinus bradycardia (6.6%). Plasma and RBCs ChE activities in OP poisoning cases were significantly decreased ($p \leq 0.01$). The activities of serum LDH and CK activities were significantly elevated ($p \leq 0.01$) in poisoning cases indicating muscular functional impairment due to OP toxicity. In a sub-set of samples, the serum levels of IgA, IgG and circulating immune complexes (C3 and C4) were also found significantly increased ($p \leq 0.01$). The findings indicated that administration of atropine with 2-PAM increases the probability of survival although the results showed no significant variation. Logistic regression analysis showed that the survival rate of the cases was about 6 times more when number of days (indirectly the quantum of atropine and 2-PAM received by the cases) increased from $<+3$ compared to >3 days. When duration of atropine administration was divided into 4 quartiles, it was observed that there is significant trend of survival of the cases (63% survival in the 1st quartile, 80% survival for 2nd quartile and 100% for 3rd and 4th quartile). The findings of this study reflect the usefulness of few clinical indices in management of OP pesticide poisoning and also support to impose the restrictions on the access of very toxic pesticides.

INTRODUCTION

Pesticides are toxic chemicals by design and their ingestion is a common cause of self poisoning in the developing world (1). The poisoning due to these chemicals is more often observed with organophosphate (OP) compounds which are easily available and often stored in an improper manner due to lack of awareness of their hazards. There are many such poisoning episodes reported from different parts of the world and also from India (2,3,4,5). Acute toxicity of OP compounds manifests as a cholinergic crisis and diagnosis is based on the clinical signs and symptoms as well as the measurement of inhibition of erythrocyte (RBC) and/or plasma cholinesterase (ChE) activities (6). There are reports that pesticide toxicity results suppression of humoral immunity

in rodents (7,8). However, the information about the influence of pesticides on the human immune system is limited. An increase of activated T-cells has been described in subjects exposed to chlorpyrifos (9). Since exposure of pesticides in the occupational settings may contribute to modulation of the immune system, the involvement of immune biomarkers in pesticide toxicity studies appears to be of considerable value (10,11). In our study, we evaluated 121 patients who were admitted to the Out Door Patient Department of B.J. Medical College and Civil Hospital, Ahmedabad – 380016, India with the diagnosis of OP poisoning and discussed the clinical and laboratory findings including immunological profile and also our experiences on the management of poisoning.

MATERIALS AND METHODS

A total 121 OP poisoning cases (aged: 14 - 72 years; male to female ratio = 1.8:1) admitted to Outdoor Patient Department of B.J. Medical College and Civil Hospital, Ahmedabad – 380016, India were studied retrospectively. The control subjects (n = 40) from hospital staff e.g. administrative staff, ward boys, nurses etc after ruling out any clinical disease matched on age and socioeconomic status with no history of poisoning were also enrolled. Information on age, sex, residential address, socioeconomic status, education, history of marital life, psychological problems, major illness, past hospitalization, family disturbances and symptoms observed during hospitalization etc. were recorded in pre-coded proforma. Complete occupational history was also noted on subjects belonging to industrial background. History of present illness at the time of admission i.e. presenting complaints and symptoms observed during hospitalization and medication, if any, were also noted. In suicidal attempts and/or accidental cases, characterization of the agents was attempted on the basis of a container shown by the patient or family members. The clinical examination as per the proforma consists of general and systemic examination including neurological examination, respiratory, cardiovascular system (including electrocardiogram recording) and gastrointestinal system. A sample of venous blood sample was withdrawn from each patient for laboratory investigations. Plasma and RBC ChE activities were estimated according to the procedure of Voss and Sachsse (12). The activities of serum lactate dehydrogenase (LDH) and creatinekinase (CK) were measured by spectrophotometric methods (13,14). Serum IgG, IgM, IgA and circulating immune complements (C₃ and C₄) were analyzed by single radial immunodiffusion technique (15).

Data are presented as Mean ± SD. SPSS software was used to calculate t-test for significance levels between the control and poisoning cases and linear regression was used for studying various relationships. Two sided p values were calculated throughout. P values ≤ 0.05 were considered significant.

RESULTS

Data on frequency distribution of age and sex in control group and OP poisoning patients are given in Table 1 and 2 respectively. Poisoning group comprised of 65.3% males and 34.7% females. The youngest case in the present study was a 14 year female and the oldest was 72 year male. About 67% cases were educated (matriculate and higher secondary

passed) and remaining were illiterate. It was noted that suicidal and intentional poisoning were the reasons in 80% cases followed by occupational (9.1%), accidental (6.6%), homicidal (1.6%) and unknown (2.5%). Social and domestic problems accounted as a major precipitating factor (29.9%) followed by marital friction (13.4%), financial stress (11.3%), love affairs (11.3%), unemployment (8.2%), chronic illness (3.1%), failure in examination (3.1%) and unknown (19.6%).

Figure 1

Table 1: Frequency distribution of age in control and OP poisoning cases.

Age group (years)	Control group		OP poisoning cases	
	n	%	n	%
10-19	10	25.0	28	23.1
20-29	23	57.5	60	49.6
30-39	6	15.0	22	18.2
40-49	1	2.5	7	5.8
≥ 50	-	-	4	3.3
Total	40	100.0	121	100.0

Figure 2

Table 2: Frequency distribution of sex in control and OP poisoning cases.

Gender	Control group		OP poisoning cases	
	n	%	n	%
Male	28	70	79	65.3
Female	12	30	42	34.7
Total	40	100	40	100

The main signs and symptoms reported by the poisoning cases were muscarinic manifestations such as vomiting (97.4%), nausea (78.4%), pinpoint pupil (66.1%), salivation (62.5%), blurring of vision (54.6%), abdominal cramps (35.6%), increased bronchial secretion (21.6%), excessive sweating (7.5%), bradycardia (6.6%), hypotension (2.4%) and cyanosis (2.4%). Nicotinic manifestations such as tachycardia (24%), hypertension (10.8%) and muscular twitching (1.8%) were also reported in these cases. The frequency of CNS manifestations was as dizziness (95.1%), headache (81.8%), mental confusion (43.1%), coma (1.6%) and convulsions (0.8%). ECG changes that were recorded before administration of atropine are shown in Table 3. Sinus tachycardia (24%) was the most common ECG abnormality followed by depression of ST segment and inversion of T wave (7.4%) and sinus bradycardia (6.6%).

Figure 3

Table 3: ECG changes in OP poisoning cases.

ECG changes	No. of cases	%
Normal ECG	75	62.0
B. Abnormal ECG		
Sinus tachycardia	29	24
Depression of ST segment and inversion of T wave in lead II, III and avF	9	7.4
Sinus bradycardia	8	6.6

Data in Table 4 indicate that plasma and RBC ChE activities in OP poisoning cases were significantly decreased ($p \leq 0.01$) as compared to controls. However, the depression was more marked in the patients who could not be survived. Serum LDH activity was significantly elevated ($p \leq 0.01$) in poisoning cases indicating muscular functional impairment due to OP toxicity. Levels of serum CK activity in a sub-sample of randomly selected OP poisoning cases ($n=36$) and control subjects ($n=20$) are depicted in Table 5. The CK activity was significantly increased in poisoning cases ($p \leq 0.01$) and comparatively marked elevation was observed among the expired patients. Levels of serum immunological profile (IgG, IgA and IgM) and circulating immune complexes (Complements C_3 and C_4) in a subgroup of OP poisoning cases ($n=21$) and control group ($n=19$) are given in Table 6. Significant rise in serum levels of IgA, IgG, C_3 and C_4 was noticed in the poisoning cases ($p \leq 0.01$).

Figure 4

Table 4: Levels of plasma and RBC ChE and LDH activities in control and OP poisoning cases.

Groups	Plasma ChE (Klett units)	RBC ChE (Klett units)	LDH (IU/L)
Control (n = 40)	70.7 ± 6.62	62.3 ± 6.2	145.6 ± 48.7
Survived OP Cases (n = 105)	48.8 ± 18.5**	41.2 ± 17.6**	217.0 ± 81.9**
Expired OP Cases (n = 16)	41.6 ± 13.0**	38.0 ± 18.6**	268.11 ± 107.69**

Data represented as mean ± SD; ** $p \leq 0.01$

Figure 5

Table 5: Levels of serum creatine kinase (CK) activity in control and OP poisoning cases.

Groups	CK (IU/L)
Control (n = 10)	72.0 ± 20.16
Survived OP Cases (n = 24)	104.0 ± 15.6**
Expired OP Cases (n = 12)	379.0 ± 53.7**

Data represented as mean ± SD; ** $p \leq 0.01$

Figure 6

Table 6: Levels of IgG, IgA, IgM, and circulating immune complexes (complements C₃ and C₄) in control and OP poisoning cases.

Parameters	Control group (n=19)	Survived OP Poisoning Cases (n=21)
IgG (mg %)	1601.5 ± 289.9	2378.3 ± 832.5**
IgA (mg %)	209.2 ± 63.2	324.2 ± 111.34**
IgM (mg %)	243.2 ± 98.45	262.5 ± 84.2
C ₃ (mg %)	84.6 ± 5.83	92.6 ± 7.32**
C ₄ (mg %)	38.86 ± 4.15	42.8 ± 4.68**

Data represented as mean ± SD, **p ≤ 0.01

Data on treatment schedule of poisoning cases have been depicted in Table 7.

Figure 7

Table 7: Treatment schedule of OP poisoning cases.

	No. of cases	Survival	Death
Atropine and 2-PAM	98	85 (86.7%)	13 (13.3%)
Atropine	18	15 (83.3%)	3 (16.7%)

Data in parenthesis indicate percentage.

In the present study, atropine with 2-PAM were administered in 98 cases and 18 cases were treated with atropine only. Five cases amongst the survival group received no treatment and only clinically observed. The findings indicated that administration of atropine with 2-PAM increases the probability of survival although the results showed no significant variation. Duration of hospital stay varies from a minimum of one day to 12 days. To study the effect of duration of stay (indirectly the quantum of atropine and 2-PAM received by the cases) was divided into two categories say <+3 days or > than 3 days. Logistic regression analysis was carried out using survival/death as dependent variable and age, sex, number of days for the dose of atropine/2-PAM/both atropine with 2-PAM administered were independent variables. It was found that the survival rate was about 6 times more when number of days increased

from <+3 compared to >3 days. However, stepwise logistic regression analysis revealed that age, sex and 2-PAM were not contributing to the patient's outcome. When duration of atropine administration was divided into 4 quartiles, it was observed that there is significant trend of survival of the cases (63% survival in the 1st quartile, 80% survival for 2nd quartile and 100% for 3rd and 4th quartile).

DISCUSSION

The diagnosis of OP poisoning was based essentially on the clinical assessment, followed by laboratory investigations. Maximum survival have been recorded in patients to whom the medical care was provided within 2 hours of consuming the poison, while mortality was noticed when medical care was delayed beyond 8 hours. However, it could be dependent or influenced by the quantum of exposure and toxicity of insecticide. Out of 121 poisoning cases, 16 subjects (13.2%) could not be survived. ECG abnormalities in form of sinus tachycardia (24%) followed by depression of ST segment and inversion of T wave (7.4%) and sinus bradycardia (6.6%) in patients were recorded which find support by the other studies (16,17).

Significant depression in plasma and RBC ChE activities in poisoning cases was observed and it offers the useful information on clinical state of the patients (18).

Organophosphates bind and inhibit ChE and their acute toxicity manifests as a cholinergic crisis with excessive glandular secretions, altered mental status, and weakness. Cholinesterase activity correlates well with the amount of pesticides absorbed in the organism and its inhibition level is also related with toxic manifestations in the body. It was apparent the depression of ChE activity was marked in those exposed subjects showing specific gastrointestinal and cardio-respiratory symptoms and supported with other findings (19). The mechanism by which OP compounds induce cardio-toxicity is still uncertain. The cardiac toxicity associated with OP poisoning is caused by more than one mechanism. Possible mechanisms include sympathetic and parasympathetic over-activity, hypoxemia, acidosis, electrolyte derangements and a direct toxic effect of the compounds on the myocardium.

Serum LDH activity was significantly elevated in poisoning cases indicating muscle functional impairment due to OP toxicity. LDH activity is directly linked with the glucose metabolism. It is very widely distributed enzyme being found in all organs of our body, but is especially plentiful in cardiac and skeletal muscle, liver, kidney and red blood

cells. The CK activity was significantly elevated in poisoning cases and more significant alterations in the patients who died due to poisoning indicating the cardiac functional impairment due to OP poisoning. It is presumed that estimation of CK activity in suspected OP poisoning cases may serve as a corroborative diagnostic parameter, along with alterations in LDH activity when associated with the changes seen in the cholinesterase activity, which is the most important biochemical change seen in OP poisoning cases. An experimental study on rats with soman, an OP, indicated depression in tissues ChE activity accompanied by concurrent increase in serum CPK activity and thus postulating the possible relationship between the different neuromuscular syndromes occurring in the course of an OP poisoning (20).

In sub-set of study population, the serum level of IgG, IgA and circulating immune complexes (C₃ and C₄) in the OP poisoning cases were significantly increased. Exposure to pesticides can cause a number of effects on the immune system varying from a slight modulation of immune functions to the development of clinical immune diseases (21). Like most other toxic compounds, pesticides are the substances that possess non-protein nature but can combine with protein to form complexes that may be antigenic and cause immunological impairment (8,11). Our previous studies on the pesticide formulators exposed to combination of pesticides in industrial settings and pesticide sprayers in field conditions indicated significant positive correlation in serum IgM and serum residue of the pesticide (Hexachlorocyclohexane; HCH) content (22,23). The findings may suggest that pesticide induced damage to the immune system may be associated with diverse pathological conditions, some of which may manifest after a long latency. Moreover, individual differences in endocrine function and nutritional balance, both of which are known to modulate the immune system, are likely to affect susceptibility to pesticide induced immune toxicity. Although the low sample size on the parameters pertaining to immunological profile (IgG, IgA, C₃ and C₄) limits the power to precisely estimate the impairment, however, it may offer some diagnostic value of clinical importance in pesticide poisoning cases.

In the present study, the treatment of the patients was based on minimizing the absorption, induction of vomiting or gastric lavage, and specific pharmacological treatment. Logistic regression analysis was carried out using survival/death as dependent variable and age, sex, number of days the dose of atropine/2-PAM/both atropine with 2-PAM

administered were independent variables. By applying logistic regression analysis, it was observed that the survival rate of the cases was about 6 times more when number of days (indirectly the quantum of atropine and 2-PAM received by the cases) increased from <+3 compared to >3 days. When duration of atropine administration was divided into 4 quartiles, it was observed that there is significant trend of survival of the patients i.e. (63% survival in the 1st quartile, 80% survival for 2nd quartile and 100% for 3rd and 4th quartile). The findings of this study highlight the usefulness of few clinical indices in the management of OP pesticide poisoning cases and also advocate the restrictions on the access of very toxic pesticides through national policies and enforcement. In addition, the strategies on integrated pest management, appropriate medical management, and early recognition of this complication, increasing the awareness of pesticide toxicity would reduce the incidence of poisoning.

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