E:/Biomedica Vol.24, Jul. – Dec. 2008/Bio-13.Doc (WC) P. 124-129

ORGANOPHOSPHATE POISONING IN THE URBAN POPULATION; STUDY CONDUCTED AT NATIONAL POISON CONTROL CENTER, KARACHI

AFTAB TURABI[1], A. DANYAL[2], SAUD HASAN[3], ASIF DURRANI[4] AND MANSOOR AHMED[5]
[1]*Department of Pharmacology, Islamabad Medical and Dental College, Main Murree Road, Barakaho, Islamabad*
[2]*Frontier Medical College, Abbottabad,* [3]*DOW Medical College, DUHS, 4Department of Microbiology, BMSI, JPMC and 5Department of Pharmacognosy, Research Institute of Pharmaceutical Sciences, University of Karachi*

The present study was performed to evaluate the patients suffered from pesticide poisoning during four years (1999-2002). The study conducted at National Poison Control Center, Karachi. The patients were categorized according to the severity of poisoning ranges from mild, moderate to severe and designated as A, B and C. Laboratory tests included blood complete picture, serum urea, creatinine, electrolyte and serum cholinesterase. S. Cholinesterase was checked on zero day of admission, repeated after 24 hrs., 3rd day, 5th day and 7th day. The results revealed that 44.97% had S. Cholinesterase level below the normal value, 33.21% landed within threshold range while 13.10% had their value above 10000 IU/ml. Other parameters showed altered haemoglobin, WBC count and S. Electrolytes. We suggest that the need of the day in developing countries is to educate the people, launch programs to change their attitude, train them regarding the safety profiles of pesticide use and implementation of law in true sense.

INTRODUCTION

Thousands of formulations and hundreds of active ingredients are used to control agricultural pests and disease carrying vectors in the world.[1] World Health Organization (WHO) has classified the toxic effects of pesticides into extremely hazardous (class Ia) to slightly hazardous (class III).[2] Most class Ia pesticides have been banned in industrialized countries, however these are freely being used in developing countries.[3]

Pesticide poisoning from occupational, accidental and intentional exposure is a major public health problem of the world. In 1990, Jeyaratnam estimated that self harm resulted in 2 million cases of poisoning each year with 200,000 deaths, while accidental and occupational exposure were estimated to cause 1 million cases with 20,000 deaths.[4] The Global Burden of Disease study estimated that 798,000 people died from deliberate self-harm in 1990, over 75% of them were from developing countries. More recent estimates of WHO reported that over 500,000 people died from self-harm in Southeast Asia and Western Pacific during the years 2000 alone.[5]

Pesticide poisoning suicide and accidental deaths and morbidity due to farming are common in South Asia. Suicide is the commonest cause of death in young Chinese women and Bangladeshi women and Sri Lankan men and women and pesticides are usually the most common mode of suicide among these populations.[6-8]

Organophosphates can be absorbed via ingestion, inhalation and dermal contact. Most of the ill-health following exposure to organophosphate is attributed to the inhibition of cholinesterase and it causes a sequential triphasic illness. Effects may appear as early as 10 minutes to as late as two hours post-exposure to 7-21 days depending on the amount absorbed and type of response. In most instances earliest cholinergic phase may only be observed. This cholinergic phase progresses to the intermediate syndrome in ~20% of subjects and both these phases are associated with high risk of mortality. Final phase of organophosphate induced delayed-polyneuropathy develops which does not carry the risk of death and may not precede by either cholinergic phase or the intermediate syndrome.[9,10]

Mild symptoms, (muscarinic) include malaise, vomiting, diarrhoea or loose stools, sweating, abdominal pain, salivation, meiosis, depression of cholinesterase level (20-40%). Moderate symptoms, (muscarinic and nicotinic) include above mentioned symptoms plus dyspnea, decreased muscular strength, bronchospasm, speech impairment, muscle fasciculation, tremours, motor incoordination, bradycardia, involuntary urination/defecation, muscular cramps, hypotension/hypertension, depression of cholinesterase in red blood cells (40-60%). Severe symptoms, (muscarinic, nicotinic and central nervous system) include symptoms of moderate poisoning plus coma, respiratory para-

lysis, extreme hypersecretion, cyanosis, sustained hypotension, extreme muscle weakness, muscular paralysis, convulsions, behavioral changes and depression of RBC cholinesterase (>60%).[11]

The use of organophosphate pesticides in Pakistan is very common and includes Dimethoate, Methamedophos, Isothioate as active ingredients. These are classified under organophosphate insecticides.[12] Very little is known about the burden of organosphosphate poisoning in Pakistan.

We analysed the patients suffered from organophosphate poisoning prospectively during four-year (1999-2002) and they visited national poison control center located in Jin-nah Postgraduate Medical Center, Karachi.

METHODS

NPCC is the National Center for registry, information, investigation, treatment and research of poisoning, located at Jinnah Postgraduate Medical Center, Karachi under Federal Ministry of Health, Pakistan and has a technical collaboration with W.H.O. This center caters people suffering from different poisonings from whole of Sindh and Baluchistan province. The center comprises of 50 beds, an ICU, trained medical & paramedical staff and clinical toxicologist. It provides services to the people free of cost in terms of expertise, medications, medical and surgical interventional procedures as required along with all diagnostic tools i.e. laboratory and radiology.

All the patients admitted to poison control center during January 1999 to December 2002 were analysed. History was taken from them or their attendants and

Table 1: *Comparative study of OP Poisoning with other chemicals in patients admitted in NPCC during January 1999- December 2002.*

(Class) Chemicals	Male	Female	Total
(I) Organophosphate	1004 (60.11%)	995 (59.79%)	1999 (59.96%)
(II) Corrosives	208 (12.45%)	213 (12.80%)	421 (12.63%)
(III) Rodenticides	104 (6.22%)	113 (6.79%)	217 (6.51%)
(IV) Kerosene Oil	27 (1.61%)	37 (2.22%)	64 (1.92%)
(V) Naphthalene	4 (0.23%)	3 (0.18%)	7 (0.21%)
(VI) Alcohol	38 (2.27%)	0	38 (1.14%)
(VII) Drug overdose	281 (16.80%)	307 (18.44%)	588 (17.63%)
Total	1670 (100%)	1664 (100%)	3334 (100%)

Table 2: *Age and Gender distribution of subjects with OP poisoning admitted in NPCC during January 1999- December 2002.*

	Male (n = 1004)	Female (n = 995)	Total (n = 1999)
Age (years)			
8 – 14	40 (3.98%)	73 (7.33%)	113 (5.65%)
15 - 20	448 (44.62%)	447 (44.92%)	895 (44.77%)
21 - 30	377 (37.54%)	287 (28.84%)	664 (33.21%)
31 - 40	89 (8.86%)	109 (10.95%)	198 (9.90%)
41^{+}	50 (4.98%)	79 (7.93%)	129 (6.45%)

Table 3: *Medico legal status, route of administration and prognosis of subjects with OP poisoning during January 1999 – December 2002.*

	Male (n = 1004)	Female (n = 995)	Total (n = 1999)
Medico legal status			
Suicidal	699 (69.62%)	649 (65.23%)	1348 (67.43%)
Accidental	305 (30.38%)	346 (34.77%)	651 (32.57%)
Homicidal	0	0	0
Route of administration			
Ingestion	792 (78.88%)	810 (81.41%)	1602 (80.14%)
Inhalation	125 (12.45%)	64 (6.43%)	189 (9.45%)
Dermal	82 (8.17%)	121 (12.16%)	203 (10.16%)
Parental	5 (0.50%)	0	5 (0.25%)
Outcome			
Mortality	53 (5.28%)	39 (3.92%)	92 (4.60%)
LAMA	18 (1.79%)	33 (3.32%)	51 (2.55%)
Recovery	933 (92.93%)	923 (92.76%)	1856 (92.85%)

their medico legal status was determined with the intent of poisoning as accidental, suicidal and homicidal. Clinical examination of the patient was conducted to determine muscle fasciculation, salivation, crepts in chest, pupil size, gut motility and level of consciousness (GCS). The patients were catego-rised according to the severity of poisoning ranges from mild, moderate to severe and designated as A, B & C. Laboratory tests included blood complete picture (CP), serum urea, createnine, electrolyte and serum cholinesterase. Serum cholinesterase level was checked on the zero day of admission, repeated after 24 hours, 3rd day, 5th day and 7th day. TDX drug analyser, serum Butyryl Cholinesterase kit, Randox laboratories Ltd. UK was used for the estimation of serum cholinesterase level.

No patient was treated as out patient. According to the protocol observed at NPCC, all patients reported the with his-tory of poisoning were kept as in patients for 24 -36 hours at least.

Patients were managed using standard protocol and general measures were taken for all patients: nothing oral (NPO), gastric lavage, oxygen (as per requirement), nasogastric tube, Foley's self retained catheter, antibiotics and diazepam (as per requirement). Specific measures taken for patients included: Pralidoxime, Atropine and Glycopyrolate administration and mechanical ventilator in a few cases.

Table 4: *Clinical groups categorized according to the severity of signs and symptoms of OP poisoning.*

Group	Males (n =1004)	Females (n = 995)	Total (n = 1999)
A (mild)	629 (62.65%)	646 (64.92%)	1275 (63.78%)
B (moderate)	225 (22.41%)	237 (23.82%)	462 (23.11%)
C (severe)	150 (14.94%)	112 (11.26%)	262 (13.11%)

Table 5: *Signs and symptoms observed among patients of OP poisoning.*

Signs and Symptoms	Males (n =1004)	Females (n = 995)	Total (n = 1999)
Increased gut sounds	1004 (100%)	995 (100%)	1999 (100%)
Increase salivation	854 (85.05%)	883 (88.74%)	1737 (86.89%)
Decreased pupils size (meiosis)	779 (77.58%)	758 (76.18%)	1537 (76.88%)
Altered consciousness	629 (62.64%)	646 (64.92%)	1275 (63.78%)
Fasciculation	629 (62.64%)	646 (64.92%)	1275 (63.78%)
Pulmonary basal crepitation	225 (22.41%)	237 (23.81%)	462 (23.11%)

Table 6: *Laboratory data for OP poisoning patients (n = 1999).*

Laboratory results	Normal	Altered
Hemoglobin (%)	1247 (62.38%)	752 (37.61%)
White blood cells count	724 (36.21%)	1258 (62.93%)
Blood sugar (mg %)	1499 (74.98%)	500 (25.01%)
Serum electrolytes (mEq/L)	724 (36.21%)	1275 (63.78%)
Serum urea (mg/dl)	1999 (100%)	0
Serum creatinine (mg/dl)	1999 (100%)	0
Serum cholinesterase (IU/L)	262 (13.10%)	1737 (86.89%)

Table 7: *Serum cholinesterase level for organophosphate poisoning among patient admitted Poison control center during January 1999 – December 2002. (Normal Range: 4500-10500 IU/ml, Threshold Range: 4500 - 5500).*

Serum Cholinesterase Level (IU /ml)	Patients
< 4500	899 (44.97%)
4500 – 5500	664 (33.21%)
5500 – 10000	174 (8.70%)
>10000	262 (13.10%)
Total	1999 (100%)

RESULTS

Among the total 3334 chemical poisoning cases, 1999 (59.96%) patients were admitted due to organophosphate poisoning. Drug overdose (17.63%) and corrosives (12.63%) poisoning were the next common poisoning. Rodenticides (6.51%) and kerosene oil (1.92%) were the less common cause of poisoning. About two percent of poisoning cases among males were due to alcohol (Table 1).

Among the 1999 patients admitted due to organophosphate poisoning, about 50% each were males (1004) and females (995). Same pattern was observed in all other poisonings. Age group most affected in between 15 – 20 years (44.77%), whereas the age group between 21 – 30 years (33.21%) was next infrequency (Table 2).

Regarding medico-legal status, suicidal incidences seem to be on the top of the list i.e 67.43%, accidental constitutes 32.57%. As regard the routes of exposure; ingestion (80.14%) was the commonest modus operandi, other routes of exposure were dermal, and inhalation. Very few cases (0.25%) were exposed through parental route. The prognosis was found to be extremely good, i.e 92.85% were completely recovered at the time of discharge. Death ensues in 4.6% whereas 2.55% of cases left the ward unnoticed against medical advice (Table 3). Among the 1999 patients of organophosphate poisoning 1275 (63.78%) fell in group A of clinical severity whereas 23.11% in group B and 13.11% in group C (Table-4 and 5). Laboratory data of these patients revealed that 44.97% had serum cholinesterase level below the normal value, 33.21% landed within the threshold range while 13.10% of cases had their values above 10000 IU/ml. Other blood parameters showed altered haemoglobin, WBC count and serum electrolytes (Table 6 and 7).

DISCUSSION

Organophosphate poisoning (OPP) is a major problem worldwide, especially in developing countries, with millions of cases and hundreds of thousands of deaths occurring each year.[13,14] Overall case fatality ranges from 10% to 20%,[15,16] particularly in rural areas. In a recent study from China reported a nationally representative sample of 518 suicides, 62% of deaths were due to pesticide ingestion and only 27% to physical methods.[17] In Sri Lanka, pesticide deaths as a percentage of total deaths by poisoning represent 77% in 2001.[18]

In parts of the developing world, pesticide poisoning causes more deaths than infectious diseases. Use of pesticides is poorly regulated and often dangerous; their easy availability also makes them a popular method in harming individual. In 1985, the UN Food and Agriculture Organisation (FAO) produced a voluntary code of conduct for the pesticide industry in an attempt to limit the harmful effects of pesticides. Unfortunately, a lack of adequate government resources in the developing world makes this code ineffective, and thousands of deaths continue to occur today.

Organophosphate insecticides inhibit acetyl cholinesterase (AChE) and cholinesterase enzymes resulting in over stimulation at cholinergic synapses.[14] The differences in the clinical courses depend on the properties of the different OP insecticide and their effect on decrease of AChE activity. As known, SChE is subject to high degree of variation induced by hereditary deficiency of this enzyme, liver dysfunction, malnutrition, iron deficiency anaemia, drugs such as cocaine, morphine, codeine, and succinylcholine, making this enzyme a less-than-perfect biomarker for OPP if baseline levels are unknown in an individual.[19,20] In fact, Nouira et al.[21] reported in their study including 30 patients that the SChE levels at admission have no prognostic value in acute OPP. It follows that measurement of EAChE, which reflects inhibition at muscarinic and nicotinic synapses, would yield a more reliable and clinically significant result with better correlation in terms of clinical presentation.[20, 2] In our study, clinical signs and symptoms that include seizures, excessive body secretions, coma, hypoxaemia, bradycardia, respiratory failure and hypotension were mostly associated with a decreease of SAChE activity. Besides, death was significantly associated with a profound decrease of the SAChE activity. On the other hand, we found no definite correlations between muscarinic and nicotinic signs and symptoms and SAChE activity. In fact and as reported by Bissbort et al[20] and Lotti,[23] central nervous system depression and early respiratory failure were associated with high decrease of EAChE. The EAChE decrease was correlated to high risks of later neurologic complications,[22,24-26] pancreatitis,[27] and mortality.[28]

Severity can be the evaluated by neurological disturbances based on different scores and investigations. In fact, the monitoring of GCS score was used by Grmec et al[29] as a marker of prognosis, that allows an early and effective triage in OPP patients. In the study of Thiermann et al,[22] the investigation of neuromuscular transmission was used as a parameter which reflects the AChE status at the synaptic site. In another study, the authors concluded that brain single photon emission computed tomography is a highly sensitive diagnostic method, together with clinical symptoms and SChE activity, for monitoring the clinical prognosis of OPP.[30] Our study conclude that coma, hypoxaemia, and haemodynamic disturbances are associated with a decrease of SAChE activity less than 4500 IU/L. The decrease of the SAChE was remarkable in comatosed patients with a depression of more than 50% of baseline value i.e. < 4500 IU/L. However, in 13.1% of cases (262 patients) we have normal SAChE value although they showed the sign % symptoms of poisoning.

According to our results we reached the conclusion that pralidoxime should be indicated only in

critically ill patients with significant decrease in their SAChE i.e. < 50% of base line value. Senanayake study group, which reported no difference in outcome in Sri Lanka when pralidoxime was unavailable in their hospital.[16] Same results were found in our study where we found the good prognosis with atropine alone along with general clinical support.

Most pesticide deaths recorded in hospital surveys are the result of self-poisoning.[31] In our study of pesticide poisoning 67.43% were of suicidal attempt. The age group most affected is between 15-20 years having almost equal gender distribution and constitutes 44.77%. Probably this age group is most frustrated and vulnerable emotionally as majority of them exposed themselves intentionally. Pakistan is also in the list of developing countries where suicidal tendency is growing tremendously. Unfortunately there is no national level data available. NPCC is the only center which is registering and maintaining the data of poisoned patients.

However, concentration on self-poisoning risks ignoring the illness and death that result from occupational and accidental exposure.[32,33] In this prospective study the accidental or occupational poisoning were 32.57%, out of which female population is slightly higher than the males as they are equally involved in the farms. Occupational illness is common because it is impractical and expensive to use safety equipment in the humid tropics.[3,33] Safety instructions written on containers are often not in native languages, many farmers are illiterate, and hence the instructions are difficult to follow. In case when farmer comes into contact with pesticides, it is not possible to "wash off at once" when there is no water available. Another important issue is the irrelevance of workers' health to employers where sick employees can be fired and new workers recruited. This attitude will continue to hinder safe practice. LAMA is the serious issue to be solved; peoples are feared from the local police who harassed them by giving threats of imprisonment especially in cases of deliberate self harm and took large bribes from their families. The other issue is of family honor especially if patient is female, most of the families tried to hide the issue for which they were forced to give bribes to police or they flew from the hospital against medical advice at the cost of their lives.

In this study, we found the rate of incidence of organophosphate poisoning in Pakistan and looked in to the age versus gender ratio, route of exposure, medico legal status and also the prognosis of these cases.

It is **concluded** that the acute organophosphate poisoning (OPP) may be monitored by the measurement of the serum cholinesterase (SChE) activities but there is no established relationship between its serum level and severity of OPP. The marked decrease of SAChE activity along with coma, respiratory failure, haemodynamic disturbances, appears in this study as prognostic factor in acute OPP. It is also recommended that the need of the day in the developing countries is; change of attitude, implementation of laws in true sense, education of people, and good governance.

ACKNOWLEDGEMENT:
The authorss acknowledge the guidance and support of Prof. Dr. Jamal Ara, National Poison Control Center, Karachi and also to Prof. Mansoor Ahmed, University of Karachi. The author is also obliged to Dr. Ahmed Danyal, Frontier Medical College, Abbottabad for his technical support in publishing this article.

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