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Analysis of Organophosphates Intoxication in a Tertiary Care Hospital.

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ABSTRACT

As the mortality rate is found to be high in organophosphorous poisoning, the study was aimed at studying the socio demographic pattern and mode of presentation of organophosphorous (OP) intoxication in Madurai, Southern Tamil Nadu. A prospective study of fifty organophosphorous compound poisoning cases, admitted through the emergency department of Government Rajaji Hospital, Madurai, were evaluated in the study. Treatment outcome was studied and reduction in cholinesterase activity was estimated to confirm the exposure and assess the severity of OP poisoning. Among the 50 cases evaluated,39 (78%) patients were males, 11(22%) were females and the mean age was 35.82 ±1.779 years. Thirty two (64%) percent of cases were illiterate and twenty six (52%) of the patients were in the lower middle socioeconomic status.Mean arrival time to the hospital after poisoning was 2.609 hours. Exposure routes were gastrointestinal in all the patients. The mortality rate was 34% and related to either the ingestion of higher doses or delay in approaching the hospital for emergency management. There was a significant reduction in serum cholinesterase level ($2.5120X10^{7}$± 1.592 mol/min/mg protein) ($P<0.05$) after OP poisoning.The extent of depression reflected the severity and was found to be reverted back towards normal upon treatment. Fatal issue is often related to causes of poisoning (suicide vs. non-suicide), delayed hospitalization and delay in diagnosis or an improper management. These findings call for a shift in emphasis in educating the masses towards first-aid care for intoxication and further necessitate the need for strict regulation of their use and adequate medical management monitoring for serum cholinesterase level will help to bring down the mortality rate.

Keywords: Organophosphorous compound, Poisoning, Suicide, Intoxication, Cholinesterase.

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INTRODUCTION

Organophosphorous (OP) compounds exhibit a high level of pest control ability combined with a relatively low grade of environmental toxicity. Hence they are used widely around the world in agriculture and in households. This has led to OP poisoning from occupational, accidental and intentional exposure which has become a major global problem [1].

OPs are irreversible inhibitors of both true or RBC cholinesterase and Pseudocholinesterase which are the biomarkers of exposure, severity and prognosis of poisoned patients. Estimation of cholinesterase level would help to confirm the exposure, severity and prognosis of patients[2]. Severe intoxication results in excessive accumulation of acetylcholine (Ach) leading to paralysis of cholinergic transmission in CNS, autonomic ganglia, parasympathetic nerve endings and neuromuscular junctions. The clinical features are due to acetylcholine over activity at muscarinic and nicotinic receptors which includes salivation, lacrimation, defecation, bronchorrhea, fasciculation and seizures. Severe poisoning may cause respiratory arrest and death through the production of excessive bronchorrhea and direct inhibition of central respiratory drive[3].

Hazardous occupational and risky storage of pesticides put safety of millions of people in jeopardy. Irrational and uncontrollable supply of these pesticides poses risk to public especially in rural areas. Promotion of necessary precautions through education and training the farmers are proving ineffective. Interestingly recognition of toxicity is resulting in paradoxical rise of such cases. Most of the villagers have stocks of these compounds at houses, readily available for deliberate self-poisoning[6]. Suicidal intake of pesticides is a huge burden on health services and causing extremely higher case fatality rate than accidental poisoning[4] .According to WHO, the world wide estimates of pesticides, number 3 million each year, with 2 million hospitalized from suicide attempts and 2, 20,000 deaths, the majority of which are actually intentional. The incidence is higher in young active males with a common fatality rate more than 10%[5].

In this study we investigated the socio-demographic pattern of organophosphorous intoxication and tried to establish the determinants which are responsible for such cases.

Patients and Methods

This is a prospective study of 50 patients of organophosphorous compound poisoning presenting at Govt. Rajaji Hospital, Madurai, Southern TamilNadu. The hospital Ethical Committee Approval was obtained to carry out the study.All cases with a history of exposure to OP poison were included in the study. Cases were admitted through emergency toxicology department and diagnosed on the basis of history of ingestion/exposure of the compound. Attendants of the patients were advised to bring the poison container. Some of them were already carrying the container with them. The informed consent from the patients or from their blood relations in case of unconscious patients was obtained before collecting the information.

While diagnosing these cases, clinical signs suggestive of muscarinic involvement like excessive salivation, sweating, miosis, and typical odour of the compound in breath and clothes were also taken into account. Finally improvement with intravenous atropine helped to confirm the diagnosis. Other agrochemicals, parquat or drug poisonings were not entertained in the study. Reduction in cholinesterase activity in serum was also estimated spectrophotometrically [6] to confirm the diagnosis and to assess the severity of poisoning. One way ANOVA followed by Student- New-man Kules Multiple Comparison test was used to analyse the significance of the continuous variable values of $P \leq 0.05$ were considered significant.

Data collected includes age, gender, education, employment and marital status, socioeconomic levels, time, dose and route of exposure of the toxic agents, frequency of different clinical features, treatment before admission, duration of hospitalization and complications. Awareness of patients about the poisonous substance was recorded and previous attempt of suicide with history of psychiatric consultation and management was also inquired.

Gastric lavage was done in all patients and atropine 2mg intravenously was given in repeated boluses until complete atropinization was achieved. Subsequently atropine was administered according to the patient's clinical situation. Pralidoxime up to 2 gm i.v stat was also administered. Severely intoxicated patients had to be put on circulatory and respiratory support.

Patients admitted with intentional intake and suicide attempt were referred for psychiatric assessment.

RESULTS

The major characteristics of 50 patients along with mode and means of exposure of poisoning is given in Table-I. The youngest patient was 18 years of age and the oldest was 70.

Table-II shows the socio-economic class and their education levels. Majority, 26 (52%) belonged to lower middle class. More than 80% of the patients of lower class were illiterate. The precipitating factors for the use of poisoning in 49 suicidal cases included, marital friction in 32(64%), strained financial stress in 9(18%), ill health in 4(8%), job stress in 2(4%), and others in 2(4%).

Most frequently used organophosphorous compound was Dichlorophos 26(52%), followed by Methyl parathion 22(44%), Chlorpyrifos 5(10%), Fenthion 4(8%), Monochrotophos 3(6%), Quinolphos 3(6%). Out of 49 suicidal cases,7(14%) consumed ≤25 ml of poison and 1 (2%) died, while 42(84%) consumed >25 ml and 16 (32 %) died. (Table-III)

Table-IV indicates the patient arrival time to hospital after the poisoning. The time ranged from 30 minutes to 12 hours. The longer time gap between the consumption of poison and the arrival in hospital determined the increased deaths. Before arrival at hospital nearly

half of the population received some medical aid at the periphery which included gastric lavage and intravenous line. 17 patients (34%) died and all of them belonged to the suicidal group. The deaths were related to larger amounts of the poison consumed and the delayed arrival to the hospital.

A marked suppression in serum cholinesterase levels was noted among all the 50 OP poisoned cases of the study. 19 (38%) have shown severe reduction, 17 (34%) were with moderate reduction, where as in 14 (28%), the reduction was mild.

The data reveals that, there is a gradual increment in ChE levels with the course of treatment and hospital stay.

Table 1: Characteristics of 50 patients with Organophosphorous poisoning

Characteristics		No of patients (%)
gender	Males	39(78%)
	Females	11(22%)
	Male:Female ratio	3.54:1
Age(years)	10-19	3(6%)
	20-29	12(24%)
	30-39	19(38%)
	40-49	9(18%)
	50-59	4(8%)
	60-70	3(6%)
	Mean age	35.82
Mode of Exposure	Suicidal attempt	49(98%)
	Accidental	1(2%)
Means of exposure	Oral ingestion	50(100%)
Severity of poisoning	Mild	14(28%)
	Moderate	17(34%)
	Severe	19(38%)

Table 2: Correlation between socio-economic class and education level in the study population.

Class	Educational level				
	Total	Illiterate	Primary	Secondary	Graduate
Lower class	18	16 (32)	2 (4)	-	-
Lower Middle class	26	14 (28)	6 (12)	5 (10)	1 (2)
Upper Middle class	4	2 (4)	-	1 (2)	1 (2)
Upper class	2	-	1 (2)	-	1 (2)
Total	50	32 (64)	9 (18)	6 (12)	3 (6)

Table 3: Amount of poison taken in self-harm cases of Organophosphorous compound poisoning (n =49)

Quantity in milliliters	Number of Patients	No of Deaths
Total (%)	Total (%)	
Less than 25 ml(≤25ml)	7 (14)	1(2)
More than 25ml(≥25ml)	42 (84)	16(32)
Total	49 (98)	17(34)

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Table 4: Association of time taken for arrival at hospital and mortality.

Duration	Number of Patients (%)	Number of Deaths (%)
<1 hour	10 (20)	2 (4)
1-2 hour	12 (24)	2 (6)
2-3 hour	11 (22)	3 (6)
3-4 hour	2 (4)	1 (2)
4-5 hour	6(12)	3 (6)
> 5 hour	9 (18)	5 (10)
Total	50 (100)	17 (34)

Table 5: Comparison of mean ChE values

Mean ChE(x10^7 moles/min/mg protein)	**Days**				
	1	**2**	**3**	**4**	**7**
Mean ± SEM	2.5120 ± 1.592	2.5868 ± 1.295	2.6761 ± 0.8930	2.7234 ± 0.5029	3.4246 ± 0.3088

Table 6: Symptoms of OP Patients

Presenting symptoms	No of patients (%)
Muscarinic manifestations	
Bradycardia	17(34%)*
Increased secretions	36(72%)
Miosis(pin point pupil)	20(40%)*
Nicotinic Manifestation	
Fasciculations	26(52%)
Tachycardia	3(6%)
CNS Manifestations	
Depressed mental status	19(38%)
Seizure	4(8%)*
Consciousness disturbance	43(86%)*
Headache	38(76%)
Giddiness	44(88%)
Complications	
Respiratory depression	21(42%)
Respiratory Failure	15(30%)*
Intermediate syndrome	3(6%)
* Indicates the symptoms of severely poisoned patients.	

DISCUSSION

Organophosphorous compounds account for two million suicide attempts and one million accidental poisoning each year worldwide [7]. These are the most significant poisons in Asia, being both widespread and coupled with a towering mortality rate. In several areas, some pesticides have become the trendiest method of suicide, gaining unsavory reputation amongst both health-care personnel and community [8]. In agricultural areas of SriLanka, the agent

responsible for 77% of the deaths was pesticides[9]. Self-poisoning with pesticides is uncommon in urban areas.

The state of TamilNadu, Southern India is an area of intensive agricultural production; pesticide use is high and has one of the highest reported rates of pesticide poisoning. The limited resources for treating this number of patients, and the uncontrolled sales and procession of the toxic agents in most parts of the world are the key determinants of high case fatality rates. So an attempt was made to carry out a study at Govt Rajaji Hospital, Maduraia a city surrounded by atleast 400 villages to observe the socio-demographic and clinical features of organophosphorous intoxication.

In this study, most of the victims of poisoning were in the age group of 30-39 followed by 20-29 years. In a study at Ahmedabad, India, the maximum number of cases were in the age group of 21-30 years[10] and in Kamenzak study it was noted as 30-39[11]. In the study by Saadeh et al the age range was 20-30 [12]. In another small study at Jan Bozy Provincial Hospital in Lublin, most of the patients belonged to 51-60 years age group[13].

Overall male to female ratio was 3.54:1 in our study. Casey P et al [14] reports male to female ratio of 2.4:1 but Guloglu [15] found male to female ratio of 1:3.5 in his study of 170 cases, where female gender was found to be predominant. In the study by Murut Sungur et al[16] , M.Balali-mood et al [17], the male: female ratio was reported to be 1.31:1 and 2.45:1 respectively. In our study the suicidal intake of Organophosphorous was prevalent among males (76%) as compared to females (22%) which were consistent with the findings of Vander Hoek W in his Sri Lankan study [18].

Agarwal [10] found that 67.4% of the cases had the intention of committing suicide, 16.8% of the cases were the result of occupational exposure, and 15.8% of the cases were from accidental poisoning. In the study by AM Saadeh et al [12] intentional exposure accounted for 67% and it was 94.3 in the study by M.Balali-mood.[17] Our reports indicated a higher incidence of suicidal attempts of 98% and accidental exposure accounted for only 1%.

In our study, more than half of the patients were married (74%) and males were found to be more prone to self harm as compared to females. Total cases who took poison due to disturbed marital life were 32. These results are different from what has been observed in other countries. For example in Southeast Anatolian region of Turkey, OP intoxication especially affected young unmarried females, and most of them resulted from a suicidal purpose[15].

Maximum patients belonged to lower middle class and only 5 patients were having qualifications up to secondary school level or above .None of the cases had previous history of suicide in the past and previous history of psychiatric illness. In cases of Kara, most of them had a primary education level (66.7%) and a lower socioeconomic status (58.3%)[19]. Hence illiteracy and poverty are also major factors to compel the people to commit suicide[20].

In this study, quantity of poison ingested and time interval between poisoning and arrival at hospital were directly linked to the death. 7 patients took more than 25 ml of the liquid and only one of them died, 42 patients consumed > 25 ml of poison and 16 of them died. In the same manner eleven patients reached hospital with a delay of >4 hours and 8 of them died. In a study conducted in Kashmir 90 percent had consumed 5 to 50 ml of organophosphates; the rest had taken more. About 80 percent were identified within two to four hours. Nine patients died, and 155 recovered. [21]. In Yuzuncu Yil University Medical Faculty Hospital, Turkey the patients' mean arrival time to the hospital after poisoning was 4.4± 3.7 (1-15) hours and in that study only four (4.7%) of them died[22]. In our study the mortality rate was 34% which was higher than that reported by Sheu JJ (23%) in Taiwan[23][3]

Among the symptomatology the most marked muscarinic signs in our study population were miosis (40%), excessive secretions (32%) and respiratory distress (42%). Most of the patients had Bradycardia (34%) at the time of admission.The most prominent of the nicotinic effect is fasciculation, which was seen in 52% of patients. Conscious disturbance; giddiness and headache were more frequently reported. Respiratory failure is the most troublesome complication in OP intoxication and it accounted for 30% mortality in our study. Similar findings have been reported by Murut Sungur et al [16]. and the mortality due to respiratory failure in his study was 29.7%

In Kara IH study, according to ECG examination, tachycardia (14, 58.3%), ST changes (13, 54.2%), and T changes (3, 12.5%) were mostly seen; bradycardia and serious ventricular arrhythmias were not seen in any case[19] which was contradictory to our study since bradycardia was seen in 34% of patients. In the study by B.Teague et al[24]., tachycardia occurred in 35% of patients and bradycardia in 28% of patients.

Inhibition of Cholinesterase enzyme activity results in acetylcholine accumulation and thereby leading to impaired neuromuscular transmission. In acute poisonings, manifestations generally occur only after more than 50% of ChE is inhibited; the severity of symptoms parallels the degree of ChE activity.

Our results were consistent with number of studies on relationship between ChE levels and acute OP poisoning which includes findings by Banerjee BD et al[25], Mahmet Tanrisev et al[26], MA Cherian et al[27], Ulrich Holfman et al[28] and Amit Tyagi et al[2].

In the study patients, ChE levels were significantly reduced at the time of admission [from 8.2104(control group) to 2.5120 x 10^7 moles /min/mg protein] and have shown a gradual remission with proper treatment. The ChE levels in severely poisoned patients were 0.512x10^7 moles/min/mg protein which was significantly ($P < 0.001$) lower than the healthy control group.

A progressive fall in ChE levels significantly correlated with severity of poisoning, and the extent to which the ChE levels are depressed reflects the clinical condition of patients. From our observation, it can be suggested that estimation of serum cholinesterase levels would be

extremely useful to identify the patients' clinical well being, especially in severely poisoned patients or comatosed patients where it is difficult to differentiate the clinical manifestations. The time interval between poisoning and treatment is very crucial in the prognosis of such cases. The limited resources in government hospitals in terms of trained doctors, nurses, support personnel, laboratory facilities and finance may be partially responsible for the high number of deaths. Greater numbers of prospective studies are needed to determine whether dedicated staff, training and evidence based protocols can lead to significant decrease in hospital mortality. Improving the availability of antidotes and implementation of well programmed emergency medical system could bring down the death rate. Firm rules and regulations concerning the trade, delivery and storage of such chemicals should be followed in order to reduce the incidence of poisoning and resulting mortality. Further, discussions should be opened with the State Agricultural Ministry, concerning targeted bans of pesticides.

CONCLUSION

The death in poisoning cases depended on a variety of factors like the Organophosphorous substance and quantity taken, the duration between poisoning and hospitalization. Illiteracy, poverty and female gender are among the major inciting agent for suicidal impulsive behavior. Probability of improvement was high when the patient was taken to hospital as soon as possible. Estimation of cholinesterase level would help in appropriate and timely management of the patients. Confinement of unsafe pesticides away from houses will reduce the accessibility for impulsive act. Hopefully, non-chemical methods of pest control will put a stop to acute organophosphorous compound poisoning.

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