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STUDY OF CLINICAL PROFILE OF HOUSEHOLD AND AGRICULTURAL INSECTICIDE POISONING PATIENTS WITH REFERENCE TO SERUM CHOLINESTERASE LEVELS

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ABSTRACT

Insecticides are abused for homicidal and suicidal purpose because of their low cost, rapid action and easy availability. It was planned to study clinical profile, outcome, morbidity and mortality with reference to serum cholinesterase levels in case of organic phosphorus and carbamate insecticide poisoning in human. A total of 50 hospitalized cases of insecticide poisoning were evaluated in this study. It was observed that insecticide poisoning was most common in young males of age group 15-30 years (48%). Most common insecticide abused was organic phosphorus insecticide (74%) and were associated with increased mortality rate. Delay in hospitalisation of >2 hours was associated with increased mortality (13 cases). Serum cholinesterase level in acute organic phosphorus and carbamate poisoning was a useful marker for diagnosis but not for prognosis. Insecticide poisoning was associated with significant mortality and morbidity, and it was highest with organic phosphorus insecticide group.

KEYWORD: Organic Phosphorus, Serum Cholinesterase, Carbamates, Insecticide Poisoning

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INTRODUCTION

India being an agricultural country, insecticides used for agriculture are easily accessible to people. Due to easy accessibility, low cost and rapid action insecticides are abused for homicidal and suicidal purpose. The commonest groups of insecticides are anti-cholinesterases, which are organic phosphorus compounds and carbamates. Other insecticide classes include organic chlorines and pyrethroids. The first potent synthetic organic phosphorus anti-cholinesterase, tetraethylpyrophosphate (TEPP), was synthesized by Clermont in 1854. Since then more than 50,000 compounds have been synthesized and screened for insecticidal activity with dozens being produced commercially.[1] Organophosphate (OP) compounds have potential to irreversibly inhibit the cholin esterases, acetylcholine esterase, and neuropathy target esterase (NTE) in humans and animals. The organophosphate compounds are not only used as insecticides and pesticides, but also used as chemical warfare agents, in petroleum additives, and as industrial plasticizers. Serious human exposure leads to both muscarinic (cholinergic) hyperstimulation and nicotinic receptor stimulation. Globally, anticholinesterase insecticides kill more people each year than acute poisoning by any other poison. An estimated 200,000 die in rural Asia as intentional self-harm is common and extremely toxic organic phosphorus insecticides are widely used in agriculture.[2,3] This study was planned to assess clinical profile, outcome, morbidity and mortality with reference to serum cholinesterase levels in case of organic phosphorus and carbamate insecticide poisoning in human.

MATERIALS AND METHODS

This hospital based case study was performed in tertiary care hospital and research centre in semi-urban area, India from October 2009 to September 2011. A total of 50 cases of insecticide poisoning were studied. All subjects were interviewed, examined and investigated as a part of routine standard examination. The study was initiated after obtaining approval of the institutional Ethics Committee and patient consent. Subject having history of exposure to insecticide compound and clinical features suggestive of insecticide poisoning were included in the study. All patients aged less than 12 years and patients with double poisoning with other drugs like opioids, diazepam, and barbiturate were excluded from the study. A detailed history was taken in every case. Particular attention was paid to the nature of insecticide compound, average quantity consumed and time lapses before the patient was admitted. If the patient was in altered sensorium, history was taken through the reliable informant. A detailed general and systemic examination was done, with particular attention to following: Alertness, Pupils: Size of the pupil-Normal/Constricted/Dilated Reaction to light-Normal/Sluggish/No response Pulse rate: <60/min, 60-100/min, >100/min; Blood pressure. Increasing secretions-Respiratory tract, Gastro intestinal tract, Skin Respiratory system – Respiratory rate, type of respiration, accessory muscles of respiration in use, crepitations, rhonchi; Per abdomen-Tenderness; Central nervous system-Consciousness, power, deep tendon reflexes, fasiculations, parasthesias, neck holding. For immediate management, patients were given first aid measures, clear airway if necessary and supported ventilation if necessary. Gastric lavage was done and a part of sample preserved for biochemical analysis. Decontamination of the skin was done by changing the contaminated clothes and washing the skin with soap and water. After clinical assessment, blood samples were analysed for Haemoglobin level, Total Lymphocyte Count (TLC) and Differential Lymphocyte Count (DLC), ESR, Blood sugar, blood urea, serum creatinine, serum electrolytes and Serum Cholinesterase level. The laboratory reference range used in the present study for serum cholinesterase: 5100 to 11700 IU / Ltr. The serum cholinesterase activity was measured by kinetic/ DGKC calorimetric method, of Zydus Pathline Limited. Treatment was given as soon as the diagnosis of

insecticide poisoning was suspected.

Statistical analysis: The statistical software namely SPSS 11.0 was used for the analysis of the data, by using chi-square test, t-test. P value less than 0.05 considered as significant.

RESULTS AND DISCUSSION

In our study as shown in (table 1), maximum number of patients were seen in the age group of 15-30 years (48%), followed by 30-45 years (36%). The least number of patients were found in the group of 60-75 years. The Jeyaratnam[4] et al study showed<30 years were 803(78%), 30-60 years were177(17%) ,>60 years were 25(2.5%).In both studies insecticide poisoning was less common in the elderly, as these insecticides are in general abused by farmers who are in young to middle age group.

TABLE 1
AGE WISE DISTRIBUTION OF CASES IN STUDY GROUP

Age (Yrs)	No of cases	Percentage (%)
15 – 30	24	48
30 – 45	18	36
45 – 60	6	12
60 – 75	2	4
Total	50	100

In our study as shown in (table 2 and), males were 26(52%), females were 24(48%). Srinivas[5] et al reported 57% in males, 43% in females, of total 1035 patients Jeyaratnam[4] et al reported 745(72%) in males, 287(28%) in females, of total 1034 patients. A present study finding of male preponderance is as reported in these two studies. Compared to studies of other groups of suicidal poisoning which is common in female group, male preponderance in our study may be due to easy accessibility of these compounds to males being more involved in agriculture.

TABLE 2
SEX WISE DISTRIBUTION OF CASES IN STUDY GROUP

Sex	No of cases	Percentage (%)
Male	26	52
Female	24	48
Total	50	100

TYPE OF INSECTICIDE: As per (table 3) Patients with organic phosphorus were 37(74%), organic phosphorus and pyrethroid combination were 5(10%), carbamates were 4(8%), organic chlorines were 1(2%), pyrethroids were 3(6%) as shown in table 3. Srinivas[5] et al reported organic phosphorus in 653(63%), carbamates 6(0.5%), organic chlorines were 212(20.5%), pyrethroids were 58(5%) of total 1034 patients. Jeyaratnam[4] et al reported organic phosphorus in 786(76%), organic phosphorus and pyrethroid combination were 3(0.3%), carbamates were 14(1.4%), organic chlorines were42 (4.1%), pyrethroids were 3(0.3%) of total 1034 patients. At present and above mentioned two studies most common groups of insecticide used was organic phosphorus insecticide. In a Srinivas et al study carbamates were least frequently used, and in Jeyaratnam et al study pyrethroids were least frequently used. Though the present study coincided in most commonly used group it did not coincide with the least common group with others. This difference may be attributed to the difference in crops grown in the study areas and hence different insecticides used.

TABLE 3
INSECTICIDE WISE DISTRIBUTION OF CASES IN STUDY GROUP

Insecticide	No of cases	Percentage (%)
Organic Phosphorus	37	74
Organic Phosphorus + Pyrethroids	5	10
Carbamate	4	8
Organic chlorines	1	2
Pyrethroids	3	6
Total	50	100

SYMPTOMS*:* In this study as shown in (table 4) patients were divided into 4 groups on the basis of type of insecticide. Vomiting was present in highest number of patients, 22(44%) of patients.19 were in organic phosphorus and organic phosphorus, pyrethroid combination group, 2 were in carbamate group, 1 was in pyrethroid group. Diarrhea was present in 4(8%) of patients, all 4 patients were in organic phosphorus and organic phosphorus, pyrethroid combination group. Salivation was present in 19(38%) patients; all 19 patients were in organic phosphorus and organic phosphorus, pyrethroid combination group. Sweating was present in 13 (26%)patients, all 13 patients were inorganic phosphorus and organic phosphorus, pyrethroid combination group.
Altered Sensorium was present in 11(22%) patients, 10 patients were in organic phosphorus and organic phosphorus, pyrethroid combination group, 1 was in an organic chlorine group. Pain abdomen was present in 11(22%) patients; all patients were inorganic phosphorus, organic phosphorus and pyrethroid combination group. Seizures were present in 5(10%) patients, 4 patients were in organic phosphorus and organic phosphorus, pyrethroid combination group. 1 was in an organic chlorine group. Bradberry[6] et al in pyrethroid poisoning reported similar findings. Shuyang[7] et al in pyrethroid poisoning patients found abnormal sensations in (92%) nausea, vomiting (8%), loss of appetite (5%), dizziness (14%), general malaise (4%), headache (11%), blurred vision (2%), fatigue (10%),chest tightness (2%).In present study vomiting was present in only one patient (2%). Other symptoms were not found in the present study because of small sample size.

TABLE 4
INSECTICIDE WISE SYMPTOM PRESENT IN STUDY GROUP

Symptoms	Organic phosphorus and Organic phosphorus+ Pyrethroids	Carbamates	Organic chlorines	Pyrethroids	Total
	n=42	n=4	n=1	n=3	N=50
Vomiting	19	2	0	1	22
Diarrhoea	4	0	0	0	4
Salivation	19	0	0	0	19
Sweating	13	0	0	0	13
Altered Sensorium	11	0	1	0	12
Pain abdomen	11	0	0	0	11
Incontinence	8	0	0	0	8
Seizures	4	0	1	0	5

SIGNS: In this study as shown in (table 5), muscle weakness was present in (18%), fasiculations 21(42%), miosis 37(74%) was present. Muscle weakness, fasiculations, miosis, tachycardia and bradycardia(64%), were found in only OP patients. Hamid[8] et al study in OP patients found fasiculations in 34(42%), miosis in 66(82%).

TABLE 5
SIGNS WISE DISTRIBUTION OF CASES IN ORGANIC PHOSPHORUS AND CARBAMATE GROUPS

Signs	No of cases	Percentage
Miosis	37	74
Crepitations	13	26
Bradycardia	32	64
Tachycardia	13	26
Muscle weakness	9	18
Fasciculations	21	45

ASSOCIATION BETWEEN DELAY IN HOSPITALIZATION AND OUTCOME IN STUDY GROUP: In our study as shown in (table 6), 20 patients hospitalized within ≤ 2 Hrs after consumption was associated with 16 recovered and 4(20%) mortality. 30 patients hospitalized in > 2 Hrs after insecticide consumption was associated with 17 recovered and 13(43%) mortality. Percentage of patients expired in the group admitted >2 hours after insecticide consumption was high. Odds ratio is 3.06. Patients admitted > 2 hours post ingestion had risk of mortality three times more than patients admitted < 2 hours. The number of patients admitted > 2 Hrs were more than that of patients admitted < 2 Hrs. Kishore[11] et al reported mean pre hospitalisation delay of 14.8±10.3 hrs in recovered patients and mean pre hospitalisation the delay of 3.3±1.71 hrs in expired patients. P value >0.217 Srinivas[5] et al reported 230(22%) deaths in 1035 patients, mean duration of delay in hospitalisation was >1.5 hours. Mehta[12] et al. Al found similar results in their study on organic phosphorus poisoning patients. This could be due to the fact that there would be a longer time available for absorption of the OP leading to further decrease in SCE. Most studies support the present study finding, delay in hospitalisation leads to increase in mortality.

TABLE 6
ASSOCIATION BETWEEN DELAY IN HOSPITALIZATION AND OUTCOME IN STUDY GROUP Chi-Square = 2.94, P>0.05 Odds ratio 3.06(CI 0.71-14.10)

Delay in hospitalization (Hrs)	Outcome		Total
	Recovered	Death	
≤ 2 Hrs	16	4	20
> 2 Hrs	17	13	30
Total	33	17	50

ASSOCIATION BETWEEN INSECTICIDE AND OUTCOME IN STUDY GROUP: In our study as shown in (table 7) there were 17 deaths. Out of 37 OP patients 22 recovered and 15 (40%) mortality and out of 5 OP+P 2(40%) mortality was present. Out of 4 carbamate patients no mortality. Out of 1 organic chlorine patient no mortality. Out of 3 pyrethroid patients no mortality. No mortality was present in carbamate group, organic chlorine group, pyrethroid group. All mortality was in OP group or OP+P group. The

Jeyaratnam[4] et al study found out of 786 organic phosphorus patients 171(74%) mortality and out of 3 organic phosphorus and pyrethroid combination group no mortality**.** Out of 14 carbamate poisoning patients 1(0.4%) mortality observed. Out of 1 organic chlorine patient no mortality. Out of 3 pyrethroid patients no mortality. In this study also highest mortality was found in organic phosphorus group. No mortality was present in organic chlorine, pyrethroid group, supporting the present study. There was one death in carbamate group, contradicting the present study. Ranjith[10] et al in a study of 93 patients found deaths in 5 (5%) out of 43 organic phosphorus patients,8(8%) out of 47 carbamate patients ,1(1%) out of 3 organic chlorine patients. In this study highest mortality was seen in carbamates group, next is an organic phosphorus group, contradicting the present study. Generally mortality associated with carbamates group is rare. Mortality reported is due to delay in hospitalisation, or any complications such as aspiration pneumonia.

TABLE 7
ASSOCIATION BETWEEN INSECTICIDE AND OUTCOME IN STUDY GROUP

Insecticide	Outcome		Total
	Recovered	Death	
Organic phosphorus	22	15	37
Organic phosphorus+ Pyrethroids	3	2	5
Carbamates	4	0	4
Organic chlorines	1	0	1
Pyrethroids	3	0	3
Total	33	17	50

Chi-Square = 4.91, P>0.05

COMPARISON OF SCE & OUTCOME IN ORGANIC PHOSPHORUS AND CARBAMATE GROUPS: In our study as shown in **(table 8)**, patients who recovered had a mean SCE level of 2183±1607 U/L, expired patients had a mean SCE level of 2237 ±1218. P Value >0.05. Our study findings demonstrate that there is no association between SCE level and outcome of the patient. Kishore[11] et al reported patients recovered had a mean SCE level of 4092±4704.2, expired patients had a mean SCE level of 3900±4617.P Value >0.65. Mehta et al[12] reported similar patterns in their study wherein two patients with severe suppression (values of < 10 % SCE) could survive. A. Dua et al[13] studied 43 patients of OP poisoning and found that neither the mortalities nor the clinical severity correlate with SCE levels. This indicates that there is no relation between mortality and the trends of changes in levels of SCE.

TABLE 8
COMPARISON OF SCE & OUTCOME IN ORGANIC PHOSPHORUS AND CARBAMATE GROUPS

Parameters	Outcome		t Value	P Value
	Recovered	Death		
	Mean ± SD (n=29)	Mean ± SD (n=17)		
SCE U/L	2183±1607	2237 ±1218	0.121	>0.05

COMPLICATION PRESENT IN STUDY GROUP: In present study as shown in (table 9), 15(30%) patients developed complications, and was associated with 6(40%) recovered and 9(60%) mortality. Aspiration pneumonia developed in 8(16%), was associated with 3(37%) recovered and 5(63%) mortality. Intermediate syndrome developed in 3(6%), was associated with 2(66%) recovered and 1(34%) mortality. Ventilator associated pneumonia developed in 4(8%), was associated with 1(25%) recovery and 3(75%) mortality. Aspiration pneumonia was the most common complication. Ventilator associated pneumonia was the complication with highest mortality rate of 75%. Cherian[173] et al described intermediate syndrome in 36(65%) of patients and infections in 25(45%) out 55 patients; they described 16 mortality in 55 patients. Vikram[15] et al described IMS in (29%) The higher incidence of IMS in some studies may be due to patients being exposed to different group of OP compounds like dimethoxy Ops, as it is more common in them. Murat[162] et al. reported complications in 35 (74.4%) patients. Respiratory failure (14 patients), aspiration pneumonia (10 patients), urinary system infection (6 patients), convulsion (4 patients) and septic shock (1 patient) out of 47 patients Ramesha[16] et al described aspiration pneumonia in 2 patients, nosocomial pneumonia in 1 patient, septicemia in 3 patients out of 9 patients who expired in a total of 49 patients. The findings of our study coincide with the above studies.

TABLE 9
ASSOCIATION BETWEEN COMPLICATIONS IN DIFFERENT INSECTICIDE GROUPS

Insecticide	Complication				Total
	Aspiration pneumonia	Intermediate syndrome	Ventilator associated pneumonia	No	
Organic phosphorus	7	3	4	22	36
Organic phosphorus+ Pyrethroids	1	0	0	4	5
Carbamates	0	0	0	4	4
Organic chlorines	0	0	0	2	2
Pyrethroids	0	0	0	3	3
Total	8	3	4	35	50

Chi-square = 5.61, P>0.05

CONCLUSIONS

Insecticide poisoning was associated with wide clinical features ranging from vomiting, miosis to convulsions and intermediate syndrome. Serum cholinesterase levels in acute organic phosphorus and carbamate poisoning was a useful marker for diagnosis but not for prognosis. Insecticide poisoning was associated with significant mortality and morbidity, highest with organic phosphorus insecticide group; also associated with delay in hospitalisation.

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