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Clinical and Biochemical Profile of Acute Organophosphorus Poisoning

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ABSTRACT

INTRODUCTION: *Poisoning is one among the common causes of causalities dealt by an emergency department physician where Organophosphorous compound (OPC) and carbamate poisoning are one among the top causes in the list witnessed in a wide variety of clinical scenarios1,2. Acute organophosphorus (OP) poisoning is a major global clinical problem, with more than thousands of deaths occurring in each year3.*

AIM: *a) To study the prevalence of OP poisoning in Coimbatore Medical College and Hospital. b) To study the clinical presentations of OP poisoning in relation to severity and outcome. c)To study the biochemical changes in OP poisoning within 24 hours of admission. d) To analyse the biochemical changes in relation to severity and outcome.*

METHOD:*The present study is a hospital based PROSPECTIVE study where 100 patients of Acute OP Poisoning (>12 years of age) admitted in Intensive Medical Care Unit in Coimbatore Medical College Hospital were randomly included to evaluate the aim of the study mentioned above. The biochemical parameters mainly serum cholinesterase and serum amylase were measured in Hitachi 912 auto-analyzer.*

RESULTS:*The prevalence of OP poisoning in Coimbatore medical college and hospital was 400 per year during this study period.OP poisoning constituted 20% of total poisoning cases admitted.100 patients with acute OP poisoning was randomly chosen for the study of which majority were in the age group of 21-30 years (31%). 74% of patients were within 40 years of age with male preponderance(76%) and male to female ratio was 3.16:1. Moderate degree of poisoning was seen in 50.9% patients with vomiting as major symptom(95%) followed by salivation (86%). In this study the common clinical signs were miosis followed by fasciculations. In the present study, the overall mortality was24%.The mortality was higher in age groups 31-40(31%)& above 40 years(34.6%). Among the expired, 19 patients were male and 5 patients were female.19 out of 76 male patients died (25% mortality). 5 out of 24 female patients died (20.8% mortality). The time interval between consumption of poison and hospital admission ranged from less than 1hour to more than 10 hours. There was less mortality (12.5%) in patients who came within 1 hour. Mortality was highest (37.5%) when patients were admitted after 6 hours following ingestion of pesticide. In patients who were admitted between 1 hour to 3 hours following ingestion of poison, the mortality was 7.7% and 26.5% in time interval groups 3-6 hours. Mean serum cholineserase level in survivors at admission was 3105.88 U/L whereas it was 2009.79 in non-survivors (p = 0.03). Mean serum amylase in survivors on the day of admission was 114U/L whereas it was 193U/L in non survivors (p = 0.001). Hyperglycemia was seen in 59% of all patients included in this study.*

CONCLUSIONS:*OP poisoning is the most common modes of suicidal deaths in our country.Poisoning is confirmed by biochemical investigation. Middle age groups between 20-40 years are more commonly encountered in poisoning by organophosphate compounds. There was good correlation between serum amylase and serum cholinesterase(Pseudocholinesterase-PChE) levels on admission and severity of poisoning. Serum cholinesterase levels were significantly depressed in patients who was in severe poisoning. Low levels of PChE and elevated amylase level in early stages of poisoning indicates increased mortality. In early stages of poisoning determining PChE activity will be a reliable diagnostic test. Mean PCHe activity in patients who survived was above 3105 U/L and in the patients who expired the PChE activity was around 2009U/L. This points out that enzyme levels is directly proportional to better prognosis.*

KEYWORDS : Organophosphorous poisoning, Miosis, Fasiculations, serum cholinesterase, serum amylase, hyperglycemia.

INTRODUCTION:

Poisoning is one among the common causes of causalities dealt by anemergency department physician where Organophosphorous compound (OPC) and carbamate poisoning are one among the top causes in the list witnessed in a wide variety of clinical scenarios. Vast majority of pesticides are made of OPCs and carbamate hence pesticide poisonings are the bulk of emergencies seen in a hospital[1,2].Acute organophosphorus poisoning is a major global clinical problem, with more than thousands of deaths occurring in each year[3].

The World Health Organisation published the first global estimation of pesticide poisoning in the year 1990[4]. Every year more than 3 million cases of pesticide poisonings occurring worldwide. Almost 2 lakh deaths mainly intentional and most of them are from Asian region. A study in 1999 showed that the mortality rate in this region is 10-20%[4] because of the increased availability of insecticides .China alone showed to have 170,000 estimated deaths per year due to deliberate self-poisoning by ingestion of OPC[5]. More recent study in 2007- Global distribution of fatal pesticide self-poisoning: A systematic review estimated that there are around 258,234 deaths worldwide annually because of pesticide (OPC) self-poisoning, accounting to30% of suicides globally.

Acute organophosphate poisoning is deliberate self-harm poison which is an emergency in India and a common cause of mortality[6,7]. India being predominantly an agricultural country, pesticides and insecticides are used abundantly for cultivation and access to these poisonous chemical substances by the population is easy. Among adults, incidence is more in females of all age groups and generally, those in second and third decades of life are more likely to be affected. The incidence of unintentional exposure to OPC is mostly seen in children[8].

OP poisoning also occurred by accidental exposure while spraying and by skin absorbtion and inhalation[9].The other methods of poisoning are ingestion of adulterated fruit, cooking oil, flour and contaminated cloth[9]. The food-borne outbreak of pesticide poisoning reported by Choudary et al [10],where malathion was earlier sprayed in the kitchen area.

METHODS

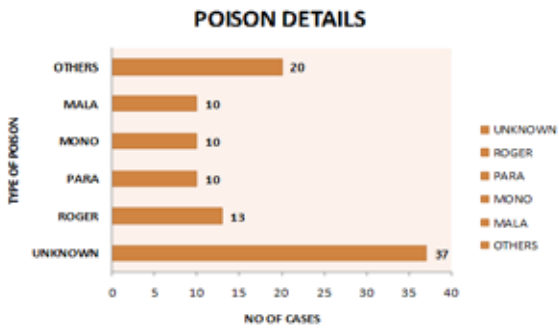
This is a Hospital based PROSPECTIVE study where 100 patients of Acute Organophosphorus Poisoning >12 years of age admitted during November 2011 to October 2012 in Intensive Medical Care Unit in Coimbatore Medical College Hospital were randomly selected to be included in the study and children <12 years of age, pregnant women, patients with Carbamate poisoning, Mixed poisoning, Liver disease, Renal failure, Coronary artery disease, Biliary disease, Pancreatic disease, Salivary gland disease, Carcinomas, DKA, Neuromuscular disorders, patients on drugs like Chemotherapy, antimalarial drugs,

codeine were excluded from the study.Serum amylase and PChE were estimated by 912 Automatic Analyzer, Hitachi,Boehringer Mannheim.

Statistics:
Descriptive statistical analysis has been carried out in thepresent study. Results on continuous measurements arepresented on Mean ± SD (Min-Max) and results on categorical measurements are presented in Number (%).Significance is assessed at 5 % level of significance. Chi-square test has been used to find the significance ofparameters on categorical scale between two or more groups.

Statistical software:The Statistical software namely SAS 9.2, SPSS 15.0, Stata10.1, MedCalc 9.0.1 ,Systat 12.0 and R environment ver.2.11.1 were used for the analysis of the data and Microsoft word andExcel have been used to generate graphs, tables etc.

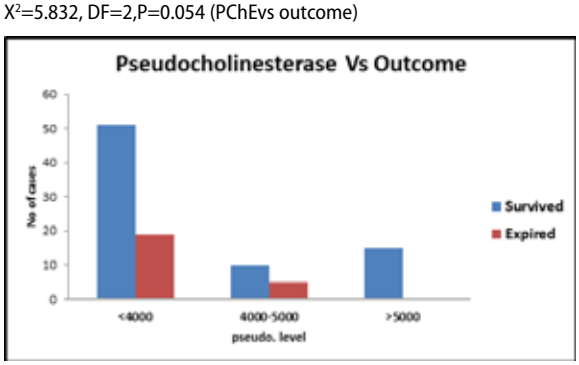
Statistical analysis:
POISON DETAILS:



PSEUDOCHOLINESTERASE (PChE) LEVEL vs OUTCOME

Pseudo level	Survived		Expired		Total
	No	%	No	%	
<4000	51	72.9	19	27.1	70
4001-5000	10	66.7	5	33.3	15
>5000	15	100	0	100	15
Total	76		24		100

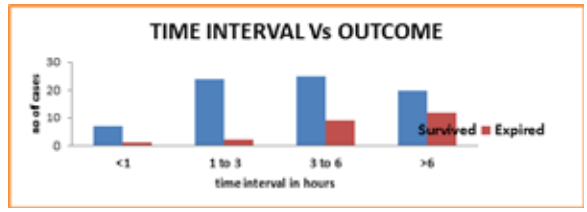
X^2=5.832, DF=2,P=0.054 (PChEvs outcome)



TIME INTERVAL vs OUTCOME:

Time interval (in hours)	Survived		Expired		Total
	No	%	No	%	
<1	7	87.5	1	12.5	8
1-3	24	92.3	2	7.7	26
3-6	25	73.5	9	26.5	34
>6	20	62.5	12	37.5	32
total	76		24		100

X^2=9.439, DF=4, P=0.051(time interval vs outcome)



SEVERITY AND PChE LEVEL:

Grade	Pseudocholinesterase level			Total
	<4000 U/L	4001-5000U/L	>5001 U/L	
Mild	35	3	8	46
Moderate	27	10	6	43
Severe	8	2	1	11
Total	70	15	15	100

X^2=5.270, DF=4, P=0.261(severity vs PChE)

BIOCHEMICAL PARAMETER vs OUTCOME:

PARAMETER	t value	p value	MEAN ± SD VALUE	
			Survived	Expired
Pseudocholinesterase	2.207	0.03	3105.88±2234.17	2009.79±1702.42
Amylase	3.808	0.001	114.15±68.46	193.20±134.95
Sugar	0.568	0.571	108.00±23.27	111.54±35.42
Urea	1.018	0.311	44.19±11.24	46.87±11.19
creatinine	0.702	0.484	1.02±0.33	1.07±0.32

SEVERITY AND SERUM AMYLASE LEVEL:

Grade	Serum Amylase		Total
	Normal	Elevated	
Mild	23	23	46
Moderate	20	23	43
Severe	4	7	11
Total	47	53	100

X^2=0.670,DF=2,P=0.715(severity vs serum amylase)

DISCUSSION
This study was conducted in Coimbatore medical college and hospital from November 2011 to October 2012. A total of 100 cases of Acute OP poisoning were studied. The clinical and diagnostic findings of this study are presented comparable with our studies in literature here.

PREVALENCE:
In our hospital, nearly 400 OP poisoning cases were admitted in one year. In a month on an average 30 cases were admitted. OP poisoning constitutes 20% of total poisoning cases. In that 2/3 cases were male patients, 1/3 were female patients. In 100 cases studied 25 cases expired due to various complications.

AGE OF THE PATIENT:
In our study, majority of patients were in the age group of 21-30 years (31%). 74% of patients were within 40 years of age. This is in comparison to studies done by Reihman et al[11], Goel et al[12]and Doshi et al[13].

GENDER DISTRIBUTION:
This study revealed a male preponderance (76%), females accounting for 24% of cases. The Male to Female ratio in this study is 3.16:1. This almost corresponds to gender distribution reported by Goelet al[12] (2.5:1).Shankar et al[14] (1.48:1), Gupta et al (2.3:1)[15].

TYPE OF POISON:
Roger and parathion was the commonly used OPC in this study which was comparable to Goelet al[12] and Avasthi et al[16] studies.

SEVERITY OF POISONING:

GRADE	Arup kumarkundu et al[17](%)	Present study(%)
MILD	19.5	46
MODERATE	50.9	43
SEVERE	29.6	11

In this study moderate degree of poisoning was 50.9% and comparable to Arup kumaret al[17] study.

CLINICAL SYMPTOMS:

SYMPTOMS	APN Kumar et al[18]	Goel et al[12]	Present study
Vomiting	93%	97.8%	95%
Salivation	87%	85%	86%
Sweating	-	-	-
Lacrimation	8.6%	-	-
convulsions	-	6.7%	-

In this study vomiting was 95% and salivation was 86% which were comparable to APN Kumar et al and Goel et al respectively.

CLINICAL SIGNS:

In this study the common clinical signs were miosis followed by fasciculations were compared to Goel et al[12], Mathur et al[19] and Reihman etal[11].

OVERALL MORTALITY:

Mortality rate in present study was 24% this is comparable to Sundaram et al[20]and Chuang et al[21]. In a reported literature the mortality rate ranges was 4 to 38%.

AGE AND MORTALITY:

In the present study, the overall mortality was 24% overall where 21.4% mortality was seen patients belonging to age group less than 20 years then 9.7% in 21-30 years age group,31% in 31-40 years age group and 34.6% in above 41 years age group. The mortality is higher in age groups 31-40 & above 40 years. Shankar et al[14]reported maximum mortality in age group of 21-30 years (61.11%). Generally younger age group are more susceptible than older group because the enzymes like mixed functions oxidases which metabolize organophosphorus compounds are less mature; but the older age group are more susceptible to complications like acute renal failure, sepsis, and multi-organ failure.

SEX AND MORTALITY:

In this study total number of deaths was 24 (24%). Among the expired, 19 patients were male and 5 patients were female.19 out of 76 male patients expired (25% mortality). 5 out of 24 female patients expired (20.8% mortality).Shankar et al[14]reported more mortality in male patients (11.6%) when compared to female patients (7.93%). Our findings are consistent with the above stated study.

TYPE OF OP COMPOUNDS AND MORTALITY:

In this study 33.3% of patients who consumed Chlorpyrifos expired. 10% in Chlorpyrifos group and 30% in parathion group expired. Mortality is high in patients who consumed compounds like monocrotophos,parathion and malathion. Our findings are consistent with studies like Shankar et al[14]and Gupta et al[15].

TIME INTERVAL AND MORTALITY:

In this study the time interval between consumption of poison and hospital admission ranged from less than 1hour to more than 10 hours. There was less mortality (12.5%) in patients who came within 1 hour. Mortality was highest (37.5%) when patients were admitted after 6 hours following ingestion of pesticide. In patients who were admitted between 1 hour to 3 hours following ingestion of poison, the mortality was 7.7%, it was 26.5% in time interval groups 3-6 hours. Our findings are consistent with Gupta et al[15] who reported increased mortality with increasing time interval between hospital admission and consumption of poison. However Karnik VM and Sunder Ram J observed no correlation between severity and time interval.

PLASMA CHOLINESTERASE AND MORTALITY:

The maximum serum cholinesterase (PChE) level at admission was 8600U/L while minimum level was 158U/L. The overall mean PChE level at admission was 2842 U/L. Mean plasma cholinesterase level in survivors at admission was 3105.88 U/L whereas it was 2009.79 in non-survivors. P value is 0.03 ($p < 0.05$) is considered as statistically significant).In majority of patients on admission it was observed that the enzyme activity was very low. Hence it can be inferred that low PChE activity can be taken as good diagnostic test for OP poisoning. Studies by Namba T et al[22]and Wadia R.S et al[23] has also shown that PChE activity estimation is a reliable diagnostic test in OPC poisoning. Observations from this study showed that patients with higher PChE activity on day of admission has a better prognosis than with lower enzyme values. Initial estimation of PChE activity can be used to predict the prognosis of patients. Recent studies by Kuppuswamy G et al showed that PChE activity below 10% of normal was associated with poor prognosis. He also observed that PChE in plasma is more sensitive than AChE to inhibition by a number of compounds and is depressed well below the normal range of 60% before any symptoms due to systemic anticholinesterase intoxication is evident. Data from patients who died showed that out of 19 patients who expired majority had enzyme value around 4000 U/L, which is lower limit of normal value. These observations shows that lower the levels of enzyme at admission the more is the mortality.

SERUM AMYLASE AND MORTALITY:

The minimum serum amylase level at admission was 35 units while maximum level was 468 U/L. The overall mean serum amylase level at admission was 94.5U/L. Mean serum amylase in survivors on the day of admission was 114U/L whereas it was 193U/L in non survivors.This substantiates our hypothesis that in OP poisoning there is an elevation of serum amylase levels according to the degree of cholinergic stimulation. Our findings are consistent with Li Tet al[24] who demonstrated hyperamylasemia is frequent in severe OP poisoning.

BLOOD GLUCOSE &MORTALITY:

Hyperglycemia was detected in 59% of patients in this study which is comparable to observations reported by Shobha et al[25] and Sungur et al[26]. In this study it was observed that severe poisoning showed hyperglycemia.Hyperglycemiaat the time of admission was associated with complications as compared to normoglycemics.

OTHER PARAMETERS:

Complete haemogram shows leucocytosis is correlated with severe poisoning. The increased total count is due to sympathetic overactivity and enhanced demargination. This study does not show much changes in acute OP poisoning within 24 hours. Liver function test shows elevated enzymes due to midzonal necrosis. In this study, the symptoms, abnormal enzymes and elevated renal parameters are associated with acute intoxication.

CONCLUSIONS:

OP poisoning is the most common modes of suicidal deaths in our country. Poisoning is confirmed by biochemical investigation.The male to female ratio in this study is 3.1:1.Middle age groups between 20-40 years are more commonly encountered in poisoning by organophosphate compounds. Majority had consumed poison orally. Most common symptom is vomiting and salivation. Most common sign is miosis. Mortality in this study was 24%. There is higher mortality with organophosphate like monocrotophos and parathion which are categorized as highly lethal compounds.There was good correlation between serum amylase and PChE levels on admission and severity of poisoning. PChE levels were significantly depressed in patients who was in severe poisoning. Low levels of enzymes PChE and elevated amylase level in early stages of poisoning indicates increased mortality. In early stages of poisoning determining pseudocholinesterase activity form a reliable diagnostic test.Mean PChE activity in patients who survived was above 3105 U/L. In the patients who expired, the PChE activity was around 2009U/L. This points out that enzyme levels is directly proportional to better prognosis. Hyperglycemia can occur in moderate to severe OP poisoning.Other biochemical changes that occurs in moderate to severe OP poisoning were elevation in urea and creatinine.

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