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A STUDY ON ASSOCIATION OF SERUM AMYLASE LEVELS IN ASSESSING CLINICAL SEVERITY AND OUTCOME OF ORGANOPHOSPHOROUS POISONING

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ABSTRACT

Introduction*:** Poisoning by organophosphosphorous Pesticides has reached epidemic proportions in most parts of the India. There is increased incidence of elevated serum amylase levels after consumption of organophosphorus compounds. Many deaths can be prevented if we assess the severity of poison initially. ***Aims & Objectives: To estimate serum Amylase levels in acute organophosphorus compound poisoning, to find out its relationship with clinical severity and outcome. ***Material & Methods:*** A prospective cross - sectional study with 50 Patients presenting with Organophosphorous poisoning were the study subjects evaluating with clinical history and all relevant investigations as per norms. ***Results***: Of the 40 patients in our study 15 patients (37.5%) had normal serum amylase level, 25patients (62.5%) had elevated serum amylase level. Age and sex of the patients have no significant relationship with the amylase levels and strong correlation between serum amylase levels with respiratory failure with significant p(<0.01). ***Conclusion:*** Symptoms like convulsions, Severe secretions, CNS depression, Fasciculations, Respiratory failure correlated very well with increasing severity of serum Amylase levels.

KEYWORDS: OP-organophosphosphorous, PAM-Pralidoxime, serum amylase.

INTRODUCTION

Acute poisoning by organophosphosphorous Pesticides (OP) has reached epidemic proportions in most parts of the world, particularly in developing countries, where the toxicity of available poisons and paucity of appropriate medical facilities ensure a high fatality rate.

Their ease of access and socio–cultural factors plays important role in choice of OP as a self-poison and the incidence is higher in young economically active group with a common fatality ratio of 20%.[1,2,3]

According to WHO, worldwide estimates of pesticide poisoning number 3 million each year. The reported overall mortality following OP insecticide poisoning varies from 4-30% in different countries and institutions.[4]

In India, OP compounds cause more self-poisoning deaths in southern and central India. In Northern India, aluminum phosphide causes most deaths with a fatality ratio over 90%.Other Pesticides used for self –poisoning include carbamates, Organochlorines and pyrethroids.[5] Organophosphorous compounds are principally used as pesticides, and their exposure is highly prevalent in developing countries

Serum Amylase In Organophosphorous Poisoning

Various studies show that there is increased incidence of elevated serum amylase levels after consumption of organophosphorus compounds, the following mechanisms have been suggested.

a) OP pesticides increase the intra ductal pressure and exocrine pancreatic flow. The increase in pressure leads to extravasation of pancreatic fluid. This increased pancreatic exocrine flow could be due to direct cholinergic hyper stimulation of pancreatic acinar and ductal cells.
b) There is pancreatic interstitial edema, acinar cell vacuolization, hyperamylasemia and hyperlipasemia.

AIM OF THE STUDY

To estimate serum Amylase levels in acute organophosphorus compound poisoning, to find out its relationship with clinical severity and outcome.

MATERIAL AND METHODS

Subjects: Patients presenting with Organophosphorous poisoning were the study subjects-A prospective cross sectional study.

Ethical committee approval: The Ethical committee approval was obtained to carry out the study in the hospital.

Study setting: Osmania General Hospital, Hyderabad, Telangana State, India.
Study duration: 18 Months

Materials
Of a total of 50 patients with organophosphorus compound poisoning admitted to the hospital during the study period, 40 were included in the study. Study is conducted for a period of 18 months.

Controls
10 healthy (age matched) individuals were kept as control

STUDY CRITERIA
Inclusion criteria
40 patients with a history of exposure to OP poison were the study subjects

Exclusion criteria
Patients with indication of exposure to a entirely different poison other than OP poison.
Patients with double poisoning
Patients who have consumed poison along with alcohol
Patients who are chronic alcoholics
Patients with history suggestive of gall stone disease
Patients with known history of lipid disorders
History suggestive of parotid gland disease
Patients with history of lipid disorders
History suggestive of parotid gland disease
Patients with history of renal or hepatic disease
History of renal or hepatic disease

Drugs causing Pancreatitis
Azathioprine, Mercaptopurine Thiazides Frusemide, Pentamidine.

Collaborating department
Department of Biochemistry, Osmania Medical College, Hyderabad

Exposure assessment
The following parameters were analyzed for association with OP pesticide exposure.
Demography, Age, Sex, Time of admission, Economical Status, Familial Status, Reason for Consumption, Poison Particulars, Severity Grade, Symptoms after consumption.
Biochemical evaluation which includes
Serum Amylase Blood glucose, urea, creatinine and Liver function tests
Clinical Outcome, Clinical Presentations
Pupil size, Pulse rate/min, Blood pressure, Respiratory rate/min, Secretions

Sample collection
40 Patients satisfying the inclusion criteria were selected for the study. About 3 ml of venous blood were collected in two occasions from each subject first within 24 hours of consumption of poison (Sample-I) and next after 24 hours of first sample (Sample-II). Serum Amylase was estimated with the help of kit manufactured by Diasys Diagnostic Systems GmbH Alte S Strasse g 65558 Holyheim Germany by using CNP-G3 method Autoanalyser AUTOPAK. Normal serum Amylase value reference range 30-110 U/L

Statistical Analysis
Data analysis was done with the help of computer.

OBSERVATIONAL AND RESULTS
Table 1: Age distribution.

Age Group	Cases		Controls	
	No.	%	No.	%
Upto 20 years	5	12.5	1	10
21-30	16	40	3	30
31-40	14	35	4	40
41 & above	5	12.5	2	20
Total	40	100	10	100
Mea n S.D.	32.3 yrs 9.3 yrs		29.9 yrs 9.5 yrs	
'p'	0.3558 Not significant			

Table 2: Sex.

Sex	Cases		Controls	
	No.	%	No.	%
Males	26	65	7	70
Females	14	35	3	30
'p'	0.5395 Not significant			

Table 3: Clinical Features.

Clinical features	Cases	
	No.	%
Pinpoint pupil	22	55
Depressed mental status	11	27.5
Secretions		
i) Mild	3	7.5
ii) Moderate	24	60
iii) Severe	11	27.5
iv) NS	2	5
Fasciculation	12	30
Heart Rate		
i) Bradycardia	17	42.5
ii) Tachycardia	-	-
iii) Normal	23	57.5
Convulsions	1	2.5
Respiratory Failure	10	25

Table 4: Age and Amylase levels.

Age group	Amylase levels					
	I		II		I – II	
	Mean	S.D.	Mean	S.D.	Mean	S.D.
Upto 20 years	132.8	155.7	44.8	44.8	88	111.6
21-30	142.9	128.7	36.4	30.3	106.4	105.8
31-40	162.6	135.1	46.4	35	116.1	112.7
41 & above	94	28.6	30.8	22.4	63.2	17.5
'p'	0.7042 Not Significant		0.744 Not Significant		0.7146 Not Significant	

Table 5: Agents and Amylase levels.

Agents	Amylase levels					
	I		II		I – II	
	Mean	S.D.	Mean	S.D.	Mean	S.D.
Methyl Parathion	150.4	157.4	39.3	35	111.1	127.5
Bug killer liquid	125.2	98.5	44.5	39.4	80.7	85.6
Fenthion	96	106.1	34.5	24.7	61.5	81.3
Quinolphos	172.5	52.3	51.8	37.1	120.8	21.7
Monocrotophos	148	141.4	45	46.7	103	94.8
Chlorpyrifos	120	48.9	32.5	13.2	87.5	47.6
Dichlorofos	128	-	22	-	106	-

Table 6: Clinical features and Amylase levels.

Clinical features	Amylase levels					
	I		II		I – II	
	Mean	S.D.	Mean	S.D.	Mean	S.D.
Pinpoint pupil Present Absent	204.1 67	136.1 38.5	52.4 25.4	33.2 25.1	151.1 41.6	111.8 27.6
'p'	**0.0001 Significant**		**0.0009 Significant**		**0.0001 Significant**	
Depressed mental status Yes No	261 97.4	151.8 75.6	63 31.7	31 29	198 65.8	131.1 54.9
'p'	**0.0003 Significant**		**0.0023 Significant**		**0.0004 Significant**	
Secretions 1. Mild 2. Moderate 3. Severe 4. NS	83 108.9 242.2 84.5	59.2 90.6 157.5 72.8	30.3 30.3 59.7 67.5	25.7 26.8 32.3 67.2	52.7 78.6 182.5 17	33.8 67.4 135.2 5.7
'p'	**0.0168 Significant**		**0.0219 Significant**		**0.0062 Significant**	
Fasciculation Present Absent	272.3 86.6	149.9 50.8	67.5 29	33.4 24.7	204.8 57.6	127.2 17.5
'p'	0.0001 Significant		0.0001 Significant		0.0001 Significant	

Table 6: Clinical features and Amylase levels (continued).

Clinical features	Amylase levels					
	I		II		I – II	
	Mean	S.D.	Mean	S.D.	Mean	S.D.
Heart Rate 1. Bradycardia 2. Tachycardia 3. Normal	209.1 - 93.3	142.8 - 83.4	51.1 - 3 3	31.8 - 31.7	157.9 - 60.4	119.5 - 59.8
'p'	**0.0001 Significant**		**0.0321 Significant**		**0.0001 Significant**	
Convulsions Present Absent	156 142.1	- 126.9	38 40.3	- 32.9	118 101.7	- 102
'p'	-		-		-	
Respiratory Failure Yes No	297.7 90.6	151.8 50.8	69.8 30.4	36.4 24.6	227.9 60.2	126.7 37.3
'p'	**0.0001 Significant**		**0.0016 Significant**		**0.0001 Significant**	

Table 7: Outcome and Amylase levels.

Outcome	Amylase levels					
	I		II		I – II	
	Mean	S.D.	Mean	S.D.	Mean	S.D.
Alive	134.6	122	39.9	33.4	94.7	96.3
Dead	213	142	44	25.3	169	130.7
'p'	0.1762 Not Significant		0.443 Not Significant		0.1428 Not Significant	

Table 8: Clinical parameters and outcome.

Clinical features	Outcome				'p'
	Alive		Death		
	No.	No.	No.	No.	
Pinpoint pupil					
Present (2)	18	81.8	4	18.2	0..8
Absent (18)	18	100	-	-	Not significant
Depressed mental status	7	63.6	4	36.4	**0.0036**
Yes (11)	29	100	-	-	**Significant**
No (29)					
Secretions					
ix) Mild(3)	3	100	-	-	**0.0001**
x) Moderate(24	24	100	-	-	**Significant**
xi) Severe(11)	7	63.9	4	36.4	
xii) NS(2)	2	100	-	-	
Fasciculation					
Present(12	8	66.7	4	33.3	**0.0054**
Absent(28)	28	100	-	-	**Significant**

Table 8: Clinical parameters and outcome (continued).

Clinical features	Outcome				'p'
	Alive		Death		
	No.	%	No.	%	
Heart Rate					
vii) Bradycardia(17)	13	76.5	4	23.5	**0.026**
viii) Tachycardia(-)	-	-	-	-	**Significant**
ix) Normal(23)	23	100	-	-	
Convulsions					

Present(1)	-	-	1	100	
					0.1
Absent(39)	36	92.3	3	7.7	Not significant
Respiratory Failure					
Yes(10)	6	60	4	40	**0.0023**
No(30)	30	100	-	-	**Significant**

DISCUSSION

Organophosphorus poisoning often presents as a medical emergency requiring monitoring and management in intensive care unit. Management of poisoning depends on clinical severity and is assessed by clinical signs and symptoms as well as laboratory evaluation. In mild cases, the management of poisoning done by removing the patient from the area of exposure and a low dose of atropine and PAM may suffice. However in severe cases mechanical ventilation, high doses of antidotes and resuscitation become necessary.

With the ease of availability, it is not surprising that the use of OP compounds in suicide attempts has mushroomed from a disturbing early trend to being one of the commonest modes of suicidal poisoning which accounted for 100% in our study. This rate was consistent with the findings of Mahdi Balali-Mood et al[6] (94.3%) whereas it was reported to be 67% by AM. Saadeh et al.[7] There was no accidental exposure in our study.

Age, Gender Prevalence

The vast majority of poisonings followed oral ingestion of liquid form and almost for all the patients gastric lavage was immediately done. The incidence was higher (40%) in the age group of 21-30 followed by (35%)in the age group of 31-40.

The incidence of op compound ingestion is more among males when compared to female. These are consistent with the findings of Muhammet Guven et al[17] and AM Saadeh et al[7], where the mean ages were 24.1 and 23.95 respectively.

The most common reason for consumption in our study was found to be the familial stress (65%) followed by financial stress (25%).In our study Methyl parathion accounted for about 52.5% of intoxication followed by Monochrotophos with 15% followed by chlorpyrifos with 10% least being Dichlorofos with 2.5% .The commonest mode of intake was found to be poison along with water (67.5%) and the next commonest mode of consumption is the direct compound itself.

Clinical symptoms

The accumulation of ACh in nerve terminals, results in continued stimulation with subsequent paralysis of receptors and accounts for the clinical signs of muscarinic, nicotinic and CNS effects.

Both the present study, and the study by Mahdi Balali-Mood et al[6], found association between the severity of poisoning and clinical manifestations.

The most marked muscarinic signs in our study population were, miosis (55%), excessive secretions (60%), and respiratory distress (25%). The most prominent of the nicotinic effect is muscular end plate block, resulting in muscle weakness and fasciculations (30%).

The most common cardiovascular system manifestations include the Bradycardia with 42.5%.In study respiratory failure occurred in 25% of cases. The CNS symptoms, like depressed mental status was found in (27.5%) patients. Similar findings have also been reported by Murat Sungur et al[9]

In our study 90% of cases had good outcome and were alive and 10% of cases have died.

Biochemical evaluation

The biochemical (Blood sugar, Serum creatinine & urea) results have not shown much variation from the normal levels in our study which was also indicated by Mahdi Balali-Mood et al[6]

Respiratory Depression

Respiratory failure is the most common dreaded complication in organophosphorus poisoning leading to mechanical ventilation and death. In a study conducted in Japan by Sumiya MN et al[10], an increase in amylase levels above the normal range have been found in 50% of the patients who developed respiratory failure.

In a study Conducted by Lin HC et al[11], found that mean amylase levels were elevated in patients with respiratory support and serum amylase levels predicted ventilator support in OP poisoning .In the study conducted by Eddleston et al[12] reported that 24% of patients required ventilation.

Our study also showed strong correlation between serum amylase levels with respiratory failure with significant p(<0.01).

In a study of Lin HC et al[11], found that mean amylase levels were elevated in patients with respiratory support and serum amylase levels predicted ventilator support in OP poisoning.

Our study in similarity with the above mentioned studies has showed strong correlation with serum amylase levels

and respiratory failure with a significant p value indicating that measuring serum amylase levels can be used as a marker of clinical severity so that most dreaded complications like respiratory failure can be prevented and treated as early as possible.

The most troublesome complication of OP poisoning was respiratory depression which could be due to reasons such as aspiration of gastric contents, excessive secretions, pneumonia and septicemia complicating adult respiratory distress syndrome. Of the 40 patients, respiratory depression was observed in 10 (25%) cases.

Serum Amylase levels in OP poisoning

This study was conducted in 50 patients with 40 patients and 10 cases as controls. There was a significant increase in serum amylase levels in first 24 hrs of op Poisoning.

In this study, the Amylase levels were significantly elevated at the time of admission [185.2U/L] and have shown a gradual remission with proper treatment.

The mean Amylase level in severely poisoned patients was 297.7 U/L which was significantly ($P < 0.01$) higher than the healthy control group.

Our study results were in accordance with the study done by Bhardwaj et al[13] where they found that serum amylase is elevated in 47% of patients with organophosphorus poisoning.

In our study on comparing the Amylase levels in first 24 hours against control, the variations were considered to be significant ($P < 0.01$). The mean Amylase level in first 24 hours was 154 U/L which is significantly higher than the control groups.

Our study showed significant correlation between the clinical symptoms like depressed mental status, increased secretions, fasciculations, Bradycardia, respiratory failure, with outcome (Alive or Dead) with a significant p value ($p<0.01$) which is similar to study conducted by Lin HC et al.[11]

Our study has similar findings with a prospective study which was undertaken by Surjeet Singh PGIMER, Chandigarh[14] to find the incidence of hyperamylasemia in patients with OP poisoning. Of the 79 patients studied, serum Amylase was found to be elevated (> 200 S.U) in 37 patients (46.95%).

Age and sex of the patients have no significant relationship with the amylase levels in our study which is similar with other studies.

The bad bedside prognostic factors which correlated very well with serum Amylase levels in the order of increasing severity include:

i) Convulsions (Amylase – 156 U/L)
ii) Severe secretions (242 U/L)
iii) CNS depression (261 U/L)
iv) Fasciculations (272U/L)
v) Respiratory failure (297.7U/L)

Our study is very useful in primary care as it can be used for predicting severity of OP poisoning by measuring serum amylase level, we can categorize the patient according to the severity so that healthcare giver can be more vigilant regarding their treatment and day to day progression of their symptoms.

Limitations of this study

a. In this present study, patients were not subjected to CT / USG Abdomen because the study was limited to serum Amylase only.
b. Autopsy study of pancreas was not done in the view of social limitation.
c. Subsets of Amylase such as pancreatic and salivary Amylase were not estimated due to laboratory constraints.
d. Urinary Amylase was not estimated due to technical limitations

CONCLUSION

- Of the 40 patients in our study 15 patients (37.5%) had normal serum amylase level. 25patients (62.5%) had elevated serum amylase level which is very significant.
- The mean Amylase level in first 24 hours of OP poisoning was 154 U/L which is significantly higher than the control groups.
- Symptoms like convulsions, Severe secretions, CNS depression, Fasciculations, Respiratory failure correlated very well with increasing severity of serum Amylase levels.

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