A Cross Sectional Study of Proportion of Respiratory Failure in Patients with Organophosphate Poisoning in a Tertiary Care Hospital in South Kerala

Narayan Mullasseril Sankarapillai[1], Mohammed Naseem Yakoobali[2], Sreenath Sreenivasan[3]

[1, 2, 3] Department of General Medicine, Government Medical College, Thiruvananthapuram, Kerala, India.

ABSTRACT

BACKGROUND

Due to the widespread use and availability of agricultural insecticides, acute organophosphate poisoning is becoming the most common type of poisoning in Kerala. The cause of death is thought to be a confluence of increased bronchial secretion, bronchospasm, respiratory muscle dysfunction, respiratory center depression and respiratory failure. The purpose of the study is to find the proportion of respiratory failure in patients with organophosphate poisoning.

METHODS

It is a cross sectional study done in 119 consenting patients who are known cases of organophosphorous (OP) poisoning satisfying the inclusion criteria. They underwent clinical assessment and laboratory investigations to assess complications of organophosphorous poisoning. Clinical features and lab findings were recorded as per protocol.

RESULTS

65 out of 119 (54.6 %) had evidence of respiratory failure. Among these 65, 20 % succumbed to death (13). 56.5 % of males (48) and 50 % of females (17) developed respiratory failure. 72.2 % of patients more than 60 years (13) had respiratory failure. Majority of the cases were of chlorpyriphos poisoning 42 (35.3 %). 76.5 % (13) of dimethoate poisoning developed respiratory failure. 93.4 % (57) of patients with respiratory failure had elevated serum amylase levels.

CONCLUSIONS

Respiratory failure is a very common complication found in organophosphate poisoning. It is more common in males than females and its proportion increases with age. The incidence of respiratory failure is more with dimethoate. Serum amylase levels can be used as a marker for development of respiratory failure in organophosphate poisoning.

KEYWORDS

Organophosphate Poisoning, Respiratory Failure, Serum Amylase Levels

Corresponding Author:
Dr. Mohammed Naseem Yakoobali,
NAAZ, TC 48/543/1,
ARA-124, Konchiravila, Manacaud,
Thiruvananthapuram, Kerala, India.
E-mail: naseemym@gmail.com

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BACKGROUND

Deliberate self-harm (DSH) is a major health problem and mortality associated with it is very high in the developing countries. As far as South India is concerned, the wide availability and lack of rules and regulations for the sale of agrochemical pesticides, especially organophosphate compounds have resulted in its widespread use for DSH.[1]

The term "organophosphates (OP)", refers to a group of insecticides (pesticides) that exerts its chemical action on the enzyme acetylcholinesterase. Commonly used organophosphate pesticides in India are:[2] (1) Chlorpyriphos (2) Diazinon (3) Dichlorvos (4) Dimethoate (5) Ethion (6) Fenthion (7) Malathion (8) Phenthoate (9) Phorate (10) Profenofos (11) Quinalphos Methyl Parathion (13) Acephate (14) Fentrothion (15) Monocrotofos and (16) Phosphamidon.

Poisoning with organophosphates accounts for about 50 % of the total cases of suicidal deaths by poisoning. In one of two separate clinical syndromes, acute cholinergic respiratory disease or intermediate syndrome - the literature attributes most deaths to respiratory failure. Due to respiratory muscle fatigue, the delayed loss seems to be due, but its pathophysiology is not yet apparent.[3] During the acute cholinergic epidemic, multiple deaths occur within hours of pesticide intake, either before or shortly after obtaining medical care. Most are caused by acute respiratory failure due to central respiratory depression, weakening of the respiratory muscles and/or immediate pulmonary effects (bronchospasm and bronchorrhoea).

Owing to an accumulation of acetylcholine (ACh), a cholinergic crisis is an over-stimulation at a neuromuscular junction due to the lack of activity (perhaps even inhibition) of the AChE enzyme, which usually dissolves acetylcholine. The muscles avoid responding to the bombardment of ACh as a result of a cholinergic crisis, resulting in flaccid paralysis, respiratory collapse, and other signs and symptoms indicative of organophosphate poisoning. Enhanced sweating, salivation, bronchial mucus along with miosis are other signs.

OP compound poisoning is associated with various biochemical abnormalities, among which hyperamylasaemia is well documented and may be due to excessive cholinergic stimulation of pancreas. Clinical features are due to stimulation of muscarinic and nicotinic. Onset is usually within 30 min to 03 hours. This may be delayed depending on the type of OP, route of exposure and amount of systemic poison. The severity of poisoning has been graded as mild, moderate and severe. The end result may be a multi system event. Most fatality occurs within 24 hours. The purpose of this study is to find the proportion of respiratory failure in patients with organophosphate poisoning and to study the proportion of respiratory failure in patients with organophosphate poisoning admitted in medical wards of Government Medical College, Thiruvananthapuram.

METHODS

This is a cross sectional study conducted on patients admitted with organophosphate poisoning in medical wards of Government Medical College and Hospital, Thiruvananthapuram from February 2018 to 2019 (after getting ethical clearance)

Inclusion Criteria

All cases of organophosphate poisoning within 24 hours of exposure. The diagnosis of organophosphate poisoning was based on the following: (1) a history of short-term exposure or contact; (2) the characteristic clinical signs and symptoms.

Exclusion Criteria

1. Patients treated outside for the poisoning.
2. Patients with a history of pancreatitis.
3. Patients with history suggestive of gall stones diseases.
4. Patients with known history of lipid disorders.
5. History suggestive of parotid gland disease. 6.History of intake of drugs likely to produce pancreatitis such as – Azathioprine, Mercaptopurine, Thiazide, Frusemide and Pentamidine.
6. Patients with chronic cardiac disease.
7. Women on oral contraceptives and pregnant women.
8. Patients on treatment for glaucoma with echothiophate.

A detailed case history was taken as per the proforma, general physical examination and systemic examination was done soon after admission. Laboratory investigations such as complete blood count, random blood sugar, renal function test, liver function test and pseudo choline esterase test were done at the time of admission. The patients were monitored regularly until the outcome. The diagnosis was made based on history or evidence of exposure to OP compound within 24 hours. Characteristic manifestations of OP poisoning such as miosis, fasciculations, excessive salivation, improvement of signs and symptoms with administration of atropine were recorded. It was represented as the muscarinic, nicotinic, and central effects of OP poisoning.

Sample Size

Minimum sample size was calculated using the formula

$$n = 4PQ\ /$$

where, P is proportion of patients developed respiratory failure in organophosphate poisoning[4]

P = 46 %

Q = 100 – p = 54 %

D = 20 % of P = 9.2

Hence, n = 4 46 54 / = 118

Sampling Technique

Consecutive patients satisfying the inclusion and exclusion criteria for study population admitted in wards of Government Medical College and Hospital, Thiruvananthapuram were enrolled for the study till the required sample size was obtained.

Statistical Analysis

The data was entered in MS Excel. Using IBM statistical package for social sciences (SPSS), Statistics for Windows, version 27.0 (released 2020), and MedCalc 2020 (MedCalc Software), statistical analysis was performed. The data was presented using descriptive statistics for calculating sensitivity, specificity, positive predictive value, negative predictive value and other variables.

RESULTS

In the present study, proportion of respiratory failure was 54.6 % i.e. 65 out of 119 patients. In the present study, the incidence of OP poisoning was more observed in males 85 (71.40 %) than females 34 (28.6 %). F : M ratio was 1 : 2.5. Incidence of OP poisoning was more observed in the age group 51 – 60 (28.6 %). Commonest route of exposure was ingestion 114 (95.8 %) whereas skin was 5 (4.2 %). According to the present study, OP poison was usually consumed along with alcohol (33.6 %). In the present study, 40.3 % (48) out of 119 patients required ventilatory support. Tracheostomy was done in 6.7 % (8) of patients out of 119. 10.9 % patients succumbed to death in the present study.

OP agents used for poisoning in the present study were Phorate 9.2 %, Methyl parathion 10.1 %, Monocrotophos 31.1 %, Dimethoate 14.3 %, and most common agent used was Chlorpyriphos (35.3 %). 93.4 % of patients with elevated serum amylase developed respiratory failure, while only 6.6 % of patients without respiratory failure have elevated serum amylase. Mean days of hospital stay in patients with respiratory failure was 14.35 and without respiratory failure was 11.04.

S. Amylase	Frequency	Percent
≤ 115	58	48.7
> 115	61	51.3
Total	**119**	**100**

Table 1. Proportion of Patients with Elevated & Normal Serum Amylase

Serum amylase is elevated (> 115 units) in 51.3 % of patients

Age in Years	Respiratory Failure				P - Value
	Present		Absent		
	N	%	N	%	
< = 30	6	46.2	7	53.8	> 0.05
31 – 40	11	50	11	50	> 0.05
41 – 50	17	53.1	15	46.9	> 0.05
51 – 60	18	52.9	16	47.1	> 0.05
61 – 70	13	72.2	5	27.8	< 0.01
Total	**65**	**54.6**	**54**	**45.4**	**-**

Table 2. Age Wise Distribution of Respiratory Failure

Incidence of respiratory failure is more in 61 - 70 age group. In this age group it is significant.

Sex	Respiratory Failure				Total		P
	Present		Absent				
	N	%	N	%	N	%	
Male	48	56.5	37	43.5	85	100	0.522
Female	17	50	17	50	34	100	
Total	**65**	**54.6**	**54**	**45.4**	**119**	**100**	

Table 3. Gender Wise Distribution of Respiratory Failure

Incidence of respiratory failure was more in males, 56.5 % males developed respiratory failure.

Outcome	Respiratory Failure				Total		P
	Present		Absent				
	N	%	N	%	N	%	
Dead	13	100	0	0	13	100	0.000
Alive	52	49.1	54	50.9	106	100	
Total	**65**	**54.6**	**54**	**45.4**	**119**	**100**	

Table 4. Relationship between Respiratory Failure and Outcome

All the patients who died were having respiratory failure earlier in their course in hospital.

S. Amylase	Dead		Alive		Total		P
	N	%	N	%	N	%	
< = 115	4	6.9	54	93.1	58	100	0.170
> 115	9	14.8	52	85.2	61	100	
Total	**13**	**10.9**	**106**	**89.1**	**119**	**100**	

Table 5. Relationship between Serum Amylase Level and Outcome

14.8 % of patients with elevated serum amylase succumbed to death. To classify the respiratory failure the optimum cut of value of S amylase was > 109 the sensitivity was 90.77 and specificity was 90.74.

Optimum cut off Value of S. Amylase	>109
Sensitivity	90.77
Specificity	90.74

Table 6. Sensitivity and Specificity for Optimum Cut Off Value of S. Amylase to Classify Respiratory Failure

DISCUSSION

Organophosphates and carbamates are frequently used pesticides which can produce life-threatening intoxication. Well over 50,000 organophosphorus compounds have been synthesized since the first one by Clermont in 1857. All these compounds act by irreversible inactivation of acetylcholinesterase (ACh). The clinical symptoms range from the classic cholinergic syndrome to flaccid paralysis and intractable seizures. About 99 % of fatal poisoning occurs in developing countries, particularly among farm workers. Despite an increased incidence of organophosphorous insecticide poisoning, the exact micro molecular changes that take place remain elusive. Till date, atropine and oxime continue to occupy the prime position in the specific management of OP poisoning.

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 this study. This rate was consistent with the findings of Mahdi Balali Mood et al.[4] (94.3 %) whereas it was reported to be 67 % by AM Saadeh et al.[5] There was accidental exposure in our study. This alarming incidence of suicidal attempts, may be probably because of the uncontrolled sale and use of these agents all over the country.

Age and Sex Incidence

In this study male : female ratio was 2.5 : 1. This was consistent with studies of Shankar P.S. which was 3 : 2, Kamath et al. 1.2 : 1 and Gupta et al. 2.3 : 1 who reported

the organophosphate poisoning to be more common in males.[6-8] In this study, the incidence of organophosphate poisoning was more among the age group of 51 - 60 years (36.6 %). The maximum age for incidence of poisoning which were reported in other studies were as follows: Shankar and Gupta et al. was 11 - 30 years, Kamath et al. was 16 - 30 years and Doshi JC[9] was 21 - 30 years.

Clinical Symptoms

The accumulation of Ach in nerve is tenuous, results in continued stimulation with subsequent paralysis of receptors and accounts for the clinical signs of muscarinic, nicotinic and central nervous system (CNS) effects.

Both the present study, and the study by Mahdi Balali-Mood et al[4]. found association between the severity of poisoning and clinical manifestations. The most marked muscarinic signs in this study population were, excessive secretions (54.6 %), and respiratory distress (54.6 %). The most prominent of the nicotinic effect was muscular end plate block, leaning in muscle weakness and fasciculations (17 %.6). The CNS symptoms like depressed mental status was found in (44.5 %) patients.

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.[4]

Respiratory Depression

Respiratory depression, which may be attributed to causes such as aspiration of stomach juices, prolonged secretions, pneumonia and septicaemia complicating adult respiratory distress syndrome, are the most troubling complication of OP toxicity. In 65 (54.6 percent) cases, respiratory depression was observed out of 119 patients.

In extreme OP overdose, early detection of respiratory collapse, prompt endotracheal intubations and artificial ventilation is life-saving.

Serum Amylase Levels in OP Poisoning

The intraductal pressure and exocrine pancreatic flow are increased by OP insecticides. The rise in pressure contributes to pancreatic fluid extravasation. Direct cholinergic hyperstimulation of pancreatic acinar and ductal cells may be attributed to this improved pancreatic exocrine flow. In the report, at the time of entry, amylase levels were substantially elevated. It can be inferred from the findings of the present analysis that predicting the levels of amylase would be extremely helpful in determining clinical severity.

Overall Mortality

The overall mortality in organophosphate poisoning in the present study was number of cases were 119 and deaths were 13 (10.9 %) where as in the studies done by Mutalik et al.[10] number of cases were 25 and the deaths were 2 (8 %), in the studies done by Kamath et al. and Vishwanathan et al.[11] number of cases were 25 and 168 and number of deaths were 2 (8 %) and 8 (4.7 %) respectively.

Type of Organophosphorus Compound and Mortality

In this study, 14.3 % of patients who consumed Chlorpyriphos died. 11.8 % in Dimethoate group and 8.1 % in Monocrotophos group died. Mortality was high in patients who consumed dangerous compounds like Chlorpyriphos and Dimethoate. Present findings are consistent with other studies like Shankar, Gupta and Kamath.[6-8]

Time Interval and Mortality

In this study, the time interval between consumption of poison and hospital admission ranged from less than 1 hour to more than 10 hours. There was no mortality in patients who came within 1 hour. Mortality was highest (40 %) when patients were admitted after 10 hours following ingestion of pesticide. In patients who were admitted between 1 hour to 3 hours following ingestion of poison, the mortality was 4.3 %, it was 9 % in time interval groups 3 - 6 hours and 20 % in patients brought between 6 - 10 hours.

The findings are consistent with Gupta et al. who reported increased mortality with increasing time interval between hospital admission and consumption of poison. However, Karnik VM[12] and Sunder Ram J[13] observed no correlation between severity and time interval.

Serum Amylase and Mortality

Mean serum amylase level in total patients at admission was 127.46 units. In OP poisoning, there is an elevation of serum amylase levels according to the degree of cholinergic stimulation. The findings are consistent with Lee WC et a.l[14] who demonstrated that hyperamylasaemia is frequent in severe OP poisoning and the finding of hyperamylasaemia was closely related to clinical severity and presence of shock.

Sixty-one (51.26 %) patients out of 119 patients were on increased serum amylase level whereas 58 (48.7 %) patients serum amylase level was normal. Among the 61 patients, 57 (87.7 %) patients developed respiratory failure. Mean duration of hospital days in respiratory failure group was 14.35 days where as non-respiratory failure group was 11.04 days. Fifty-two (80 %) patients recovered from respiratory failure out of 65 patients. This demonstrates that greater the serum amylase level at admission, higher was the complications and prolonged the hospital stay.

CONCLUSIONS

- There is male preponderance in this study.
- Late middle age groups between 51 - 60 years were more commonly encountered in poisoning by organophosphate compounds.
- Clearly there was no age factor associated with severity

of clinical manifestations or mortality.

- There was higher mortality with organophosphate like Chlorpyriphos and Dimethoate which are categorized as highly lethal compounds.
- Hospital stay and mortality increases as the duration between ingestion of poison and hospital admission is longer.
- A significant proportion of patients developed respiratory failure.
- Respiratory complications constitute a major cause of death.
- There was a good correlation between serum amylase levels on admission and duration of hospital stay and severity of poisoning.
- There is a greater probability of the patient being ventilated if the serum amylase level at admission is more.
- There is a direct correlation between the serum amylase level on admission and the number of ventilator days.
- Serum amylase levels may be viewed as a measure of organophosphorous poisoning, as it allows early detection of severity and also helps in recognizing people at risk of causing organophosphorous poisoning complications.
- This study demonstrates a strong association between markedly elevated levels of amylase and respiratory dysfunction and bad outcomes.
- A large rise in the level of serum amylase also poses different risks including CNS depression, fasciculations, and respiratory collapse convulsions.

Small sample size was a limitation of the study.

Data sharing statement provided by the authors is available with the full text of this article at jebmh.com.
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