

USE OF CLINICAL AND BIOCHEMICAL PARAMETERS IN PREDICTION OF VENTILATOR SUPPORT IN ORGANOPHOSPHORUS COMPOUND POISONING

Umamaheshwari S¹, Hally Karibasappa¹, Vinaya Shivayogi Kohalli², Anuradha H³

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Corresponding Author:

Dr. Anuradha H,
Email: hanuradha19@yahoo.com
ORCID: 0000-0002-7957-2006

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¹Associate Professor, Department of General Medicine, Vijayanagar Institute of Medical Sciences Ballari Karnataka, India.

²Senior Resident, Department of General Medicine, Vijayanagar Institute of Medical Sciences Ballari Karnataka, India.

³Assistant Professor, Department of Anesthesia and Critical Care, Vijayanagar Institute of Medical Sciences (VIMS), Ballari Karnataka, India.

Abstract

Background: OP pesticide self-poisoning is estimated to kill many people each year in the Asia Pacific region. Hence, the present study is undertaken to identify the factors both clinical and biochemical, which help in predicting the need for ventilator support and thus helping to reduce the mortality by timely institution of it. In developing world, Poisoning is a common method of suicide. Organophosphorus poisoning is an important public health problem. To assess the prognostic significance of such clinical and biochemical parameters in predicting the need for ventilator support in OPC poisoning. **Materials and Methods:** It is a prospective descriptive study done at VIMS, Ballari, with a sample size of 50 cases. Patients who filled the inclusion criteria are assessed as per proforma specifically designed for the study. **Result:** In this study population, majority (18%) were in the age group of 21 – 30 years, males comprised 76%, 32% students, and 94% of patients consumed with intention of suicide. The most common compound (42%) used was Chlorpyrifos, mortality was highest with Monocrotophos (62%). Majority of patients (68%) admitted within 5 hours of poison consumption, and most common symptom was Vomiting (94%). In the study, 30% of the patients required ventilator support. 24% of patients had severe reduction of pseudocholinesterase values and among them 75% required ventilator support. And 100% of patients with severe poisoning according to POP scale required ventilator assistance. **Conclusion:** Clinical and biochemical parameters such as low GCS, high POP scale, increased fasciculation, low pseudocholinesterase levels were strong predictors for the need of ventilator support. Grading of the degree of the poisoning taking the above parameters into consideration can help to identify high risk patients who may go in for Respiratory failure and require ICU admission and Ventilator support.

INTRODUCTION

Worldwide an estimated 30,00,000 people are exposed to organophosphate or carbamate agents each year, with up to 3,00,000 fatalities.^[1] Toxicity usually results from intentional or accidental ingestion or exposure to agricultural pesticides. In south Indian states, insecticide poisoning is very common mainly because of their increased agricultural activities and it accounts for a significant number of admissions to ICU in this region. Easy availability and lenient rules and regulations regarding sales makes Organophosphorus compounds one of the most

commonly used means for deliberate self-harm. Accidental exposure is also common in agricultural labourers and factory workers.

OP poisoning has high inpatient mortality and many patients have cardiorespiratory arrests after admission. There is 10-20% case fatality rate in developing countries compared with much lower fatality in developed countries.^[2] So early identification and aggressive management is often important in this condition. Improved medical management and provision of antidotes and ICU beds, together with bans on the most toxic pesticides should reduce the case fatality for self-poisoning and noticeably reduce the number of deaths from self-

harm in rural asia.^[2,3,4] As many ICUs here are often overcrowded and are resource poor, it may not be fully possible to identify and properly manage patients who develop complications of OP poisoning. This scenario highlights the need for predictive prognostic markers. Hence the present study is done to identify the factors both clinical and biochemical, which will help in predicting the need for ventilator support and thus helps to reduce mortality by timely institution of ventilator support.

MATERIALS AND METHODS

This study was carried out on those 50 cases of Organophosphorus compound poisoning attending casualty and emergency ward of General Medicine, Vijayanagara Institute of Medical Sciences Ballari Karnataka. Duration of study was one year i.e December 2020 to November 2021.

Sample Size Estimation

A total of 50 patients with diagnosis of organophosphorus poisoning admitted to VIMS Medical College and Hospital during the period from December 2020 to November 2021 who were willing to participate in the study were taken as study subjects.

Calculation of Sample Size

Formula for sample size: (Source: Lwanga SK, Lameshaw S. Sample size determination in health studies WHO, Geneva, 1991) $n = Z^2 P(1-P)/d^2$ where, n = sample size, Z = Z score, P = population proportion D = Margin of error

Inclusion Criteria

Patients with Organophosphorus compound poisoning above the age of 18 years, Patients with history of poisoning of single Organophosphorus compound and Patients presenting within 24 hours of poison consumption.

Exclusion Criteria

Patients below the age of 18 years, Patients with more than one type poisoning, Patients with known neuromuscular junction disorders, Patients with chronic lung disease, Patients with known cardiac disease, Patients already treated elsewhere for poisoning, Patients presented 24 hours after the consumption of poison and Pregnancy

Method of Collection of Data

A provisional diagnosis of Organophosphorus poisoning was made on the basis of definite history of poisoning either by the patient himself or attendants, which was substantiated by

- Examination of the container
- Typical clinical features (hyper salivation, miosis and fasciculation), and or
- Characteristic odour of stomach wash and or vomitus, and

- Levels of pseudo cholinesterase.

Each patient enrolled for study underwent a detailed clinical examination as per proforma (specifically designed for the study), which includes examination for signs of respiratory failure, detailed assessment of central nervous system and cardiovascular system.

All patients were given a stomach and body wash. 5ml of blood was collected at the time admission, before initiation of treatment and the samples were sent for estimation of serum pseudocholinesterase and serum potassium apart from other routine investigations. Reference range for serum pseudocholinesterase was taken as 4260-12920 IU/L. A pseudocholinesterase activity of 40-60% of normal constituted mild poisoning, between 20-40% was taken as moderate poisoning and values less than 20% was considered as severe poisoning. The reference range for serum potassium was 3.5-5.5 mEq/l. Thereafter, a bolus dose of atropine was administered after correcting cyanosis till signs of Atropinization appeared.

This was followed by slow IV bolus dose of PAM (pralidoxime). All the patients were monitored closely and continuously in the Emergency Ward/Intensive Care Unit and all clinical signs assessed 12 hourly till complete recovery.

Ventilator support was considered in patients with - apnea or hypoventilation, persistent cyanosis, persistent tachypnea (Respiratory rate >35/min) and deranged arterial blood gases viz., $paO_2 < 50$ mm of hg, $pcO_2 > 50$ mm of hg and or acidosis ($ph < 7.2$).

Statistical analysis: Qualitative data is represented in the form of frequency and percentage. To assess the association between variables Chi Square test was used. If the cell were small Fischer's Exact test was used. A P value of <0.05 was considered statistically significant.

RESULTS

In this study, total number of patients included are 50 and maximum number of patients were 21 - 30 years (36%). Patients above 50 years constituted only 4% of the study population. Out of 50 total patients, 38 of them are males (76%), 12 of them are females (24%). Majority of the patients consumed poison with intention of suicide (94%). Only 3 patients (6%) were having accidental exposure to poison. No homicidal intention was present in the study group.

There is total 12 different Organophosphorus chemicals consumed by the patients. 21 patients (42% of study population) took Chlorpyrifos. The Second most common compound consumed was Monocrotophos, 8 people (16%).

32% of the patients were students and 20% of the patients were students and 16% were unemployed.

In this study group, only those patients who presented within 24 hours of consumption of poison.

Majority of the patients (68%) presented within 5 hours of consumption of poison. Delay in admission was about 11 to 15 hours in 2% of the patients and 8% of population presented after 15 hours.

14% of the study population had mild hypokalaemia at the time of presentation and 2% of population had

moderate hypokalaemia. In rest of the patients, serum potassium levels were normal and there is no hyperkalaemia.

20% of the patients had mild reduction in pseudo cholinesterase activity. 56% of the patients had moderate reduction and 24% had severe reduction in pseudo cholinesterase activity.

Table 1: Frequency distribution according to severity of pseudoChE reduction

Severity of Pch reduction	No of cases	Percent
Mild	10	20.0
Moderate	28	56.0
Severe	12	24.0
Total	50	100.0

In total study population, 62% of the patients had a mild poisoning of POP scale score (0 – 3), 34% of the patients had moderate poisoning of POP scale score (4 – 7) and 4% of the population had severe poisoning of POP scale score (8 – 11).

In total study population 30% of the patients required ventilator support. 70% of the patients didn't require ventilator support

Table 2: Frequency distribution of ventilator support

Ventilatory support	No of cases	Percent
YES	15	30.0
NO	35	70.0
Total	50	100.0

Of the 50 patients enrolled in the study, 38 patients (76%) improved. 12 patients (24%) died due to various complications. Of the 12 deaths, 9 deaths were due to intermediate syndrome and 3 deaths were due to Respiratory failure.

Only 3 % of the patients with mild grade of poisoning required ventilator support but 71 % of patients with moderate grade of poisoning and 100 % of patients with severe grade of poisoning required ventilator assistance. This was statistically highly significant (p value <0.001)

Of the 16 patients with mild reduction in pseudocholinesterase activity, only 1 (6%) required ventilator support. There were 19 patients with moderate reduction in serum pseudocholinesterase activity. Of these, 5(26%) required ventilator support. 12 patients had severe reduction in pseudocholinesterase and among them 9 patients(75%) ended up in ventilator support. The p value for this association was calculated as <0.001, which was highly significant.

Of the 50 patients studied, 20 patients required Atropine dose of <100mg and ventilator required in 10% of cases. 5 cases required Atropine dose of >300mg and 40% required ventilator support among them. This association was found to be significant statistically (p value <0.05).

Among 11 patients who got admitted between 6 – 10 hours of consumption, 59% of them required ventilator support. None of them required ventilator support who got admitted after 15 hours of consumption. When analysed, this association was found to be statistically non-significant (p value 0.229)

75% of the patients with monocrotophos and Dichlorvas poisoning required ventilator support. 50% of the patients with Phorate poisoning needed ventilator assistance. When analysed by Pearson Chi square test, this association was found to be statistically insignificant (p value <0.09).

Table 3: Association between compound consumed and need for ventilator support.

Compound	No of cases	Ventilatory support			
		YES		NO	
		No	%	No	%
Chlorpyrifos	21	4	20	17	85
Diazinon	3	0	0	3	100
Dichlorvas	4	3	75	1	25
Malathion	3	0	0	3	100
Monocrotofos	8	6	75	2	25
Propenofos	3	1	33	2	67
Phorate	2	1	50	1	50
Quinolofos	2	0	0	2	100
Acephate	2	0	0	2	100
Carbofuron	1	0	0	1	100
Sulphus and Quinolophus	1	0	0	1	100
Total	50	15	30	35	70
Chi Square test P<0.09, Not Sig					

Of the 42 normokalemic patients, 11(26%) required ventilator support. 7 patients had mild hypokalemia at the time of presentation and 57% of the patients needed ventilator support and 1 patient who had moderate hypokalemia required no ventilator support later in the treatment. This association was found to be statistically insignificant (p value <0.204).

Table 4: Serum potassium and ventilator support

S. Potassium	No of cases	Ventilatory support			
		YES		NO	
		No	%	No	%
Normal	42	11	26	31	74
Mild Hypokale	7	4	57	3	43
Moderate	1	0	0	1	100
Total	50	15	30	35	70

Chi Square test P<0.204, Not Sig

62% of the patients who consumed Monocrotofos compound died. Mortality was 50% in those patients who consumed Phorate and Dichlorvas. When the compounds consumed and clinical outcome were subjected to statistical analysis, the association was not found to be significant(p value <0.206).

Table 5: Association between compound consumed and clinical outcome

Compound	No of cases	Outcome			
		Died		Improved	
		No	%	No	%
Chlorpyrifos	21	3	14	18	86
Diazinon	3	0	0	3	100
Dichlorvas	4	2	50	2	50
Malathion	3	0	0	3	100
Monocrotofos	8	5	62	3	38
Propenofos	3	1	33	2	67
Phorate	2	1	50	1	50
Quinolofos	2	0	0	2	100
Acephate	2	0	0	2	100
Carbofuron	1	0	0	1	100
Sulphus and Quinolophus	1	0	0	1	100
Total	50	12	24	38	76

Chi Square test P<0.206, Not Sig

97% of the patients with mild grade poisoning in POPS scale improved. Mortality rate was 53% in moderate grade poisoning and 100% in severe poisoning. This association was found to be statistically significant (p <0.001).

All the patients with normal levels and mild reduction in pseudocholinesterase activity improved. 26% of the patients with moderate reduction and 58% of the patients with severe reduction died, which when analysed by Pearson Chi square test was found to be significant with a p value of

Table 6: POPS score and clinical outcome

POPS Score	No of cases	Outcome			
		Died		Improved	
		No	%	No	%
Mild (0- 3)	31	1	3	30	97
Moderate (4 - 7)	17	9	53	8	47
Severe (8- 11)	2	2	100	0	0
Total	50	12	24	38	76

Chi Square test P<0.001, Highly Sig

DISCUSSION

Majority of the patients in the study group were males 76% and females constituted 24%. Similar male preponderance was observed by Goel et al, and Rajeev H et al also, in their studies but in a study by Suhail Sidiq et al poisoning was more common in females (67.6%).^[5,6,7]

The most common compound consumed by patients was Chlorpyrifos (42%) followed by Monocrotofos and Dichlorvas. Study done by Rajeev H et al showed that Methyl Parathion was most common

compound used and study by Dayanand Raddy et al showed that Dimethoate was most common compound used.^[6,8] The compounds available may have regional variations according to local agriculture and economy.

In the present study, commonest symptom encountered was vomiting (94%) followed by excessive secretions. Seizures was not encountered. Whereas excessive secretion was most common symptom followed by vomiting in a study by Rajeev et al.^[9]

In our study, 62% of the patients had mild grade of poisoning according to POP scale score, 34% had moderate grade poisoning and 4% had severe poisoning. Only 3% of patients with mild grade of poisoning needed ventilator support, while 100% patients with severe poisoning required ventilator assistance. This relation was statistically highly significant. 97% of the patients with mild grade of poisoning according to POP scale improved. 100% of the patients with severe poisoning expired. These findings were similar to study by Raveendra et al, Ravi Chethan AN et al.^[9,10]

In this study 32% of the population had mild reduction of serum pseudocholinesterase values and among them 6% required ventilator support. 24% had severe reduction of pseudocholinesterase values and among them 75% required ventilator support. Rajeev et al,^[6] has demonstrating that low pseudocholinesterase level is associated with poor prognosis, mortality, longer ICU stay as well as a longer time to come out of mechanical ventilation.

Study done by Eddleston et al,^[3] has shown that different OP compounds inhibit pseudocholinesterase in varying degrees, when compared to their abilities to inhibit acetylcholinesterase. Results of

pseudocholinesterase activity should be interpreted keeping these patients in mind, although it can be taken as a good prognostic marker in our setting.

Total dose of Atropine required in 20 out of 50 patients was <100mg and 90% of them improved and in patients where >300mg of Atropine was required, 80% of them improved and 20% expired which was statistically insignificant, but patients with severe reduction in pseudocholinesterase required a much higher dose higher dose of atropine and lower levels required less amount of Atropine and improved.

D.R.Murthy et al,^[11] has shown that hypokalemia is a frequent finding in OP poisoning. Murthy et al has proposed serum potassium at the time of admission as a predictive marker of ventilator support. In a study by Prasad DR. serum potassium and pseudocholinesterases are important predictive markers.

Rajeev et al,^[6] has shown that need for mechanical ventilation was directly proportional to the mean delay in presentation. Sunderam et al^[9] reported higher mortality rate in patients who presented more than 4 hours after consumption of OPC poison.

Among 50 patients, 15 patients (30%) of the patients required ventilator support and in 15 patients 12 (80%) expired. Out of the 15 patients who required ventilator support, 12 died and 3 patients survived. None of the non-ventilator patients died. In a study done by Ayca Acikalın et al,^[12] the percentage of patients requiring ventilator support was found to be 34.2%. In a study done by Eranık KB et al,^[13] the percentage of patients requiring ventilator support was 52.85% and in them 37.1% patients expired.

Of the 50 patients enrolled in our study, 38 patients (76%) improved and 12(24%) patients died due to

various complications. The mortality rate was 16% in a study by Rajeev et al.^[6]

Out of the 12 deaths, 9 were due to intermediate syndrome and 3 were due to Respiratory failure. The cause of death in OPC poisoning, as studied by Kiran et al,^[14] showed intermediate syndrome to be the most common cause (46%), followed by ventilator associated pneumonia (26%), ARDS (8%) and MODS (8%).

In our study, mortality was highest with Monocrotophos (62%) followed by Phorate (50%) and Dichlorvos (50%). Rajeev et al^[6] reported higher death rates with Methyl parathion and Dimethoate. In a study by Eddleston et al,^[3] the toxicity and mortality rates of each compound shows a linear relationship with absorption of the compound from GIT, deposition in various tissues, pharmacokinetics and irreversible inhibition of acetyl cholinesterase.

CONCLUSION

An increased POPS score in patients with OP poisoning is associated with increased risk of respiratory failure and increases the need of ventilator support. Serum pseudocholinesterase is a useful marker for predicting clinical outcome in OP poisoning as marked reductions are associated with increased need for ventilator support. However Serum Potassium has no relation with ventilator support or outcome in this study.

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