PREDICTING THE NEED FOR VENTILATORY SUPPORT IN ORGANOPHOSPHORUS COMPOUND POISONING

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ABSTRACT

Organophosphorus compound poisoning is a major health problem not only in developing countries, but also in western countries.¹ Hospital-based statistics suggest that nearly half of the admissions to emergency with acute poisoning are due to organophosphorus compound poisoning.²

MATERIALS AND METHODS

The study was conducted on 100 patients who were diagnosed to have consumed organophosphorus compound poison admitted in M.G.M Hospital, Warangal, from April 2013 to May 2014 who were admitted within 24 hours of consumption of the poison.

RESULTS

100 patients diagnosed to have consumed organophosphorus compound poison were studied in relationship to the need for ventilatory support. In the total target study of 100 patients, 36 patients required ventilatory support.

DISCUSSION

Acute organophosphorus compound poisoning is one of the most frequent poisonings encountered in M.G.M Hospital. The major cause of poisoning in the present study was attempted suicides (100%).

CONCLUSION

The factors, which predicted the need for ventilatory support in organophosphorus compounds poisoning in our study of 100 patients. The presence of higher fasciculation score (≥ 4) was associated with the higher need for ventilatory support. A GCS score ≤ 10 was significantly associated with an increased need of ventilatory support.

KEYWORDS

Organophosphorus Poisoning, Ventilator, Atropine.

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INTRODUCTION

Organophosphorus compound poisoning is a major health problem not only in developing countries, but also in western countries.¹ Hospital-based statistics suggest that nearly half of the admissions to emergency with acute poisoning are due to organophosphorus compound poisoning.²

Organophosphorus compounds were first discovered more than 100 years ago are at present the predominant group of insecticides employed globally for pest control.³ Organophosphorus compound poisonings are found to be a leading cause of death in agricultural countries globally.⁴⁻⁵ Organophosphorus compounds poisoning affects globally approximately 3 million population and causes 2,00,000 deaths annually, most of these occur in developing countries.⁶

Organophosphorus compounds are easily available as insecticides in shops and have resulted in a gradual increase in suicidal and accidental poisoning.

Nearly 90% of the poisoning are suicidal with a fatality rate of $>10\%$. 8-10% accidental and $<1\%$ homicidal. Occupational exposure accounts for 1/5th of accidental poisoning with fatalities of $<1\%$.⁷

The organophosphorus compounds are the organic derivatives of phosphorous-containing acids. The phosphonate, which are organic derivatives of phosphoric acid are not used as insecticides, but are used as chemical warfare agents. Organophosphorus compounds combine with esteratic sites of acetyl cholinesterase that is phosphorylated and phosphorylated esteratic sites undergo hydrolysis. The phosphorylated enzyme is inactive and thus unable to hydrolyse acetylcholine. The biological effects of organophosphorus compound are as a result of accumulation of endogenous acetylcholine at sites of cholinergic transmission. This causes disruption of transmission of nerve impulses in both peripheral and central nervous system. Most organophosphorus compounds are readily absorbed through respiratory, oral mucous membrane, GIT mucous, and through intact skin as they are lipid soluble. This binding is irreversible except with early pharmacological intervention.⁸

The diagnosis is based on the history of exposure and features of cholinergic overactivity.⁹ The treatment includes atropine or glycopyrrolate, which acts as a physiological antidote, PAM, which help in reactivating the enzyme.

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Complications like respiratory failure, CNS depression, and ventricular arrhythmias should be anticipated and treated. The early causes of death in organophosphorus compound poisonings are chiefly related to ventricular arrhythmias, CNS depression, seizures, or respiratory failure due to excessive bronchial secretions, bronchospasm, pulmonary oedema, aspiration of gastric contents, paralysis of respiratory muscles, or apnoea associated with depression of the medullary respiratory center.¹⁰ Late mortality is associated with respiratory failure^{11,12} and infections like pneumonia, septicaemia, or complications related to mechanical ventilator and intensive care management.¹³ This study will help us to identify the factors, which help in predicting the need for ventilatory support in a patient with OP poisoning.

MATERIALS AND METHODS

The study was conducted on 100 patients who were diagnosed to have consumed organophosphorus compound poison admitted in M.G.M. Hospital, Warangal, from April 2013 to May 2014, who were admitted within 24 hours of consumption of the poison. The included patients were intensively monitored for signs of respiratory insufficiencies like respiratory rate of >30 breaths/minute, accessory muscles of respiration in action, O₂ saturation <90%, Arterial Blood Gas Analysis (ABG) - PaO₂ <50 mmHg, PCO₂ >50 mmHg. If any one or more are present, the decision for mechanical ventilator was taken. Bradycardia was defined as <60 beats/minute.

Patients with concomitant illness or conditions likely to alter the respiratory effort due to organophosphorus compound poisoning, patients with double poisoning with other poisons, those with chronic lung disease, and those treated outside were excluded from the study.

Based on the factors that influence the need for ventilatory support, the severity of organophosphorus compound poisoning was graded as mild, moderate, and severe poisoning.

Mild Poisoning includes

- Normal level of consciousness.
(Score of 12-15 by Glasgow coma scale (GCS)).
- Pupil size ≥ 4 mm.
- Fasciculation score 0-1.

Moderate Poisoning includes

- Mild alteration in level of consciousness.
(Score of 8-11 by GCS).
- Pupil size 2-3 mm.
- Fasciculation score 2-4.

Severe Poisoning includes

- Stupor/Coma (GCS 7 or less).
- Pinpoint pupil (1 mm or less).
- Presence of convulsions.
- Fasciculation score 5 or more.
- Signs of respiratory insufficiency.

Grading of fasciculation was done by giving 1 point depending on the presence of fasciculations each to the anterior chest, posterior chest, anterior abdomen, posterior abdomen, right thigh, left thigh, right leg, left leg, right arm, and left arm.

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RESULTS

100 patients diagnosed to have consumed organophosphorus compound poison were studied in relationship to the need for ventilatory support. In the total target study of 100 patients, 36 patients required ventilatory support.

Age in Years (N=100)	Number of Patients are Presented	Number of Patients with Ventilation	P Value	Odds Ratio Ventilation
13-20	22 (22%)	8 (8%)	P>0.05	1.02
21-30	58 (58%)	22 (22%)	0.655	1.22
>30	20 (20%)	6 (6%)	0.61	0.71

Table 1: Age Distribution with Ventilation

Majority of the patients who were ventilated were in the age group of 21-30 (58%), but this was not statistically significant (P>0.05)

Sex	Number of Presented (n=100)	Number of Patients with ventilation (n=18)	P Value
Male	60 (60%)	26 (26%)	P = 0.0855
Female	40 (40%)	10 (10%)	

Table 2: Sex Distribution with Ventilation

Male patients were 60 (60%) and females were 40 (40%).

The gender distribution among patients ventilated is not statistically significant with sex ($P>0.05$).

Compounds	Number of Patients Presented	Number of Patients with Ventilation	P Value	Odds Ratio (Ventilation)
Acephate	8 (8%)	-	-	-
Triazophos	2 (2%)	-	-	-
Dimethoate	2 (2%)	-	-	-
Malathion	2 (2%)	-	-	-
Monocrotophos	26 (26%)	13 (13%)	0.099	1.47
Temephos	2 (2%)	2 (2%)	0.617	-
Chlorpyrifos	26 (26%)	13 (13%)	0.099	1.47
Dichlorvos	16 (16%)	6 (6%)	>.05	0.72
Quinophos	4 (4%)	-	-	-
Phorate	10 (10%)	2 (2%)	0.32	0.28
Parathion	2 (2%)	-	-	-

Table 3: Relationship of Compounds Consumed with Ventilation

Of the patients who consumed organophosphorus poison, monocrotophos and chlorpyrifos were the most commonly consumed poisons (26 in each group). 50% patients who consumed these compounds required ventilatory support. Patients who consumed Dichlorvos and Phorate were least likely to receive ventilatory support. Hence, statistically patients who consumed monocrotophos and chlorpyrifos are 1.47 times more likely to receive ventilation.

Fasciculation Score (n=50)	Number of Patients Presented	Number of Patients with Ventilation	P Value	Odds Ratio (Ventilation)
0	28 (28%)	6 (6%)	0.067	0.38
1-3	40 (40%)	10 (10%)	0.0885	0.44
≥4	32 (32%)	20 (20%)	0.0017*	5.42
	** highly	Statistically significant		

Table 4: Relationship of Fasciculation Score with Ventilation

Generalised fasciculations was another conspicuous feature in 72% of cases in this study.

Patients with fasciculation score of ≤3 are less likely to receive ventilation. The patients with a fasciculation score ≥4 are 5.42 times more likely to receive ventilation.

Pupil size (n=50)	Number of Patients Presented	Number of Patients with Ventilation	P Value	Odds Ratio (Ventilation)
≤1	28 (28%)	20 (20%)	0.144	1.61
≥2	52 (52%)	16 (16%)	0.144	0.62

Table 5: Relationship of Pupil Size with Ventilation

Patients with pupil size ≤1 mm are 1.61 times more likely to require ventilation as compared to the patients with pupil size ≥2 mm. This finding is not statistically significant.

GCS-Score (n=50)	Number of Patients Presented	Number of Patients with Ventilation	P Value	Odds Ratio (Ventilation)
≤10	26 (26%)	22 (22%)	P<0.001**	23.57
11-15	74 (74%)	14 (14%)	P<0.001**	0.04

Table 6: Relationship of GCS Score with Ventilation

Seventy four (74%) patients had a GCS score of 11-15, out of these 14 (18.9%) patients required ventilatory support. Ventilatory support was required by 84.6% of patients who had a GCS score ≤10. Hence, patients with GCS score ≤10 are 23.57 times more likely to receive ventilation when compared to the patients with GCS score 11-15.

Type of Poisoning (n=50)	Number of Patients Presented	Number of Patients with Ventilation	P Value	Odds Ratio (Ventilation)
Mild	46 (46%)	10 (10%)	0.007*	0.30
Moderate	30 (30%)	10 (10%)	>.05	0.85
Severe	24 (24%)	16 (16%)	0.0006*	5.60

Table 7: Requirement of Ventilatory Support in Relation to Severity of Organophosphorus Compound Poisoning

Ten (21.7%) of the patients with mild poisoning and 33.3% of the patients with moderate poisoning required ventilatory support. In contrast, 66.6% of the patients with severe poisoning required ventilation. Hence, patients with severe poisoning were 5.6 times more likely to receive ventilation.

Time Lag (n=100)	Number of Patients Presented	Number of Patients with Ventilation
<4 hrs.	4 (4%)	-
≥4 hrs.	96 (96%)	36 (36%)

Table 8: Relationship between Time Lag of Consumption of Poison and Admission to the Hospital with Ventilatory Support

Of the patients admitted to the hospital ≥ 4 hours after consumption of poison, 36% required ventilatory support. In comparison, patients admitted < 4 hours of consumption, did not require ventilatory support. This finding is statistically significant.

Pulse rate (n=100) Beats/Mins	Number of Patients Presented	Number of Patients with Ventilation	Significance (P Value)
≤ 60	6 (6%)	2 (2%)	$P > 0.05$
61-70	62 (62%)	26 (26%)	0.136
≥ 71	32 (32%)	8 (8%)	0.126

Table 9: Relationship of Pulse Rate with Ventilation

Bradycardia was present in 6% of the cases in the present study. There is no statistical association between pulse rate and ventilation.

Respiratory Rate (n=100) Breaths/Min	Number of Patients Presented	Number of Patients with Ventilation	P Value	Odds Ratio (Ventilation)
≤ 20	60 (60%)	6 (6%)	$P < 0.001^{**}$	0.04
21-25	16 (16%)	6 (6%)	$P > 0.005$	1.08
26-30	18 (18%)	18 (18%)	$P < 0.001^{**}$	-
> 30	6 (6%)	6 (6%)	0.0016*	-

Table 10: Relationship of Respiratory Rate with Ventilation

100% of the patients with respiratory rate > 25 breaths/minute required ventilatory support, which is statistically significant with a P value < 0.001 .

Factors	No. of Patients Ventilated	No. of Patients not Ventilated	P Values	Odds Ratio (Ventilation)
Monocrotophos	13 (13%)	13 (13%)	0.099	1.47
Chlorpyrifos	13 (13%)	13 (13%)	0.099	1.47
Fasciculation score (≤ 3)	16 (16%)	52 (52%)	0.0017**	0.18
Fasciculation score (≥ 4)	20 (20%)	12 (12%)	0.0017**	5.42
Pupil size (≤ 1 mm)	20 (20%)	28 (28%)	0.3004	1.60
Pupil size ≥ 2 mm)	16 (16%)	36 (36%)	0.3004	0.62
GCS score (≤ 10)	22 (22%)	4 (4%)	$P < 0.001^{**}$	23.57
GCS score 11-15	14 (14%)	60 (60%)	$P < 0.001^{**}$	0.04
Mild poisoning	10 (10%)	36 (36%)	0.007*	0.30
Mod. poisoning	10 (10%)	20 (20%)	0.85	0.85
Severe poisoning	16 (16%)	8 (8%)	0.0006*	5.60
Time lag (< 4 hrs.)	-	4 (4%)	$P < 0.001^{**}$	-
Time lag (≥ 4 hrs.)	36 (36%)	60 (60%)	$P < 0.001^{**}$	-
Pulse rate (≤ 60 beats/min.)	2 (2%)	4 (4%)	$P > 0.05$	0.88
Pulse rate (≥ 61 beats/min.)	34 (34%)	60 (60%)	$P > 0.05$	1.13
Respiratory rate (≤ 25 breaths/min)	12 (12%)	64 (64%)	$P < 0.001^{**}$	-
Respiratory rate (> 25 breaths/min)	24 (24%)	-	$P < 0.001^{**}$	-
O ₂ Saturation ($\leq 89\%$)	36 (36%)	2 (2%)	$P < 0.001^{**}$	-
O ₂ Saturation (> 90)	-	62	$P < 0.001^{**}$	-
Accessory muscles-In action	36 (36%)	-	$P < 0.001^{**}$	-
Accessory muscles-not in action	-	64 (64%)	$P < 0.001^{**}$	-

Table 14: Factors Predicting the Need for Ventilatory Support

O ₂ Saturation (n=100)	Number of Patients Presented	Number of Patients with Ventilation
90-100%	62 (62%)	-
$\leq 89\%$	38 (38%)	36 (36%)

Table 11: Relationship of O₂ Saturation with Ventilation

Of the 38 patients who had oxygen saturation levels of $\leq 89\%$, 36 (94.73%) required ventilatory support.

Accessory Muscles	Number of Patients Presented	Number of Patients with Ventilation
Not-acting	64 (64%)	-
In action	36 (36%)	36 (36%)

Table 12: Relationship of the Use of Accessory Muscles with Ventilatory Support

38 (38%) patients had accessory muscles of respiration in action of which all required ventilatory support, this is statistically significant.

	Atropine Dose (mg) within 48 hrs.	
	Number of Patients	Mean $\pm$ SD
Ventilated	36	161.33 $\pm$ 64.31
Not ventilated	64	100.93 $\pm$ 93.12
Significance Student t	Student t=3.971 P=0.00239**	

Table 13: Relationship of Atropine Dose within 48 Hours of Admission with Ventilatory Support

Patients who were ventilated required a higher dose of atropine within 48 hours of admission as compared to those who were not ventilated. This is statistically significant.

Statistical Methods

Chi-square test and Fisher Exact test has been used to find the significance of ventilation requirement for all the study parameters. The odds ratio has been used to find the strength of relationship between the ventilation requirement and the each study parameters. Analysis of variance has been used to find the significance change of study parameters in mild, moderate, and severe type of poisoning. The Kruskal-Wallis test has been used to find the significance change of GCS score in mild, moderate, and severe type of patients as the GCS score do not follow normal distribution. Student t test has been used to find the significance of mean difference atropine within 48 hours between ventilated and not ventilated patients.

Statistical Software

The statistical software namely SPSS 10.0 and Systat 8.0 were used for the analysis of the data and Microsoft word and Excel have been used to generate.

RESULTS

Male patients were 60 (60%) and females were 40 (40%). The gender distribution among patients ventilated is not statistically significant with sex ($P > 0.05$).

DISCUSSION

Acute organophosphorus compound poisoning is one of the most frequent poisonings encountered in M.G.M. Hospital. The major cause of poisoning in the present study was attempted suicides (100%). Suicide is the major cause of poisoning in developing countries.^{7,11} In contrast figures from developed countries like Japan show accidental exposure forms a major bulk of organophosphorus compound poisoning cases.^{9,14}

Among the 100 cases studied, majority of the patients were in the age group of 21-30 years (58%). This correlates with the study done by S. Singh et al.¹⁵

In the present study, 60% of the patients were males. This correlates with the findings of the previous studies. However, in a study done by M. Vishwanathan et al,¹⁶ 66% of the patients who consumed organophosphorus compound were females.

Vomiting was the most common symptom in 80% of the patients in this study. This correlates with the studies done by OP Gupta et al,¹⁷ Sarjit Singh et al,¹⁸ and Goel et al¹⁹ where vomiting was present in 90% and 97.08% of the cases respectively. Vomiting was probably due to chemical gastritis.

Generalised fasciculations was another conspicuous feature in 72% of cases in this study. Whereas, studies done by Goel et al¹⁹ and Sarjit Singh et al²⁰ showed that 55% and 100% of the patients respectively had fasciculations. Forty eight (48%) patients had pupil size ≤ 1 mm of which 20 (41.6%) patients required ventilatory support. According to the study done by OP Gupta et al¹⁷ 28% had pupil size ≤ 1 mm who required ventilatory support. In comparison, in a study done by Robert et al¹⁸ 73% who had pupil size ≤ 1 mm required ventilation.

Bradycardia at admission was present in 6% of the cases in the present study. In comparison, in a study done by Robert et al,²⁰ 19% of the patients had bradycardia while in a study carried out by Semir Nouria²¹ 17% had bradycardia. This has

not been compared with the need for ventilation.

Twenty four (24%) patients had respiratory rate > 25 breaths/min. of which all patients required ventilatory support. The higher respiratory rate was probably due to increased secretion and more severe respiratory paralysis caused by the poison itself. According to the study done by G. S. Mutalik et al,¹⁷ 40% of the patients had a respiratory rate more than 30 breaths/min., but this has not been compared with the need for ventilation.

Thirty eight (38%) patients had oxygen saturation levels of $\leq 89\%$ out of which 36 (94.73%) patients required ventilatory support. Thirty six (36%) patients had accessory muscles of respiration in action of which all required ventilation. There are no comparative studies available.

It was observed in this study that 36% of the patient with respiratory failure required mechanical ventilation as compared to 40% of the patients in a study done by T.C. Tsao et al.¹¹ Arterial blood gas analysis was done in 36 patients who had a respiratory rate > 25 breaths/minute and whose accessory muscles of respiration were in action. All of them had respiratory acidosis.

Patients who were ventilated required a higher dose of atropine within 48 hours of admission as compared to those who were not ventilated. This was consistent with the findings of the study done by Goel et al.¹⁹ Higher dose of atropine may indirectly indicate the severity of poisoning, which might have caused respiratory paralysis requiring ventilation.

The severity of organophosphorus compound poisoning and the need for ventilatory support was studied in relationship to the nature of compounds consumed. 50% of the patients who consumed monocrotophos and 50% of the patients who consumed chlorpyrifos required ventilation in this study. Whereas, in the study done by Goel et al, 66.67% of the cases who had consumed dimethoate was associated with maximum need for ventilatory support. Ventilatory support was required by 84.6% of patients who had a GCS score level of less than 10. This correlates very well with the study done by Goel et al¹⁹ where 84% of the patients with GCS score less than 10 required ventilation.

Of the patients with fasciculation score ≥ 4 , 62.5% required ventilatory support in our study whereas in a study done by Goel et al¹⁹ 55% of the patients with a fasciculation score of more than or equal to 4 required ventilatory support.

21.7% of the patients with mild poisoning and 33.3% of the patients with moderate poisoning required ventilatory support. In contrast, 66.6% of the patients with severe poisoning required ventilation. Studies done by Goel et al¹⁹ have shown that about 4% of the patients with mild and 6% of patients with moderate poisoning required ventilator support whereas 62% of the patients with severe poisoning required ventilatory support.

The reason for greater percentage of patients requiring ventilation in mild poisoning group in our study is likely to be due to the greater time lag between poison consumption and to admission at the hospital. This in turn resulted in delay in treatment like initiation of gastric lavage and administration of atropine and PAM.

Of the patients who were admitted to the hospital after 4 hours or more after consumption of organophosphorus poison, 36% required ventilator support as compared to those who were admitted within < 4 hours of consumption.

The studies done by Goel et al 64 and S.S. Kumar et al, which indicated a very significant relationship between delay in treatment and need for ventilator support. In contrast, a study done by Karnik et al²² found this delay statistically insignificant.

CONCLUSION

The factors which predicted the need for ventilatory support in organophosphorus compounds poisoning in our study of 100 patients were as follows:

1. The presence of higher fasciculation score (≥ 4) was associated with the higher need for ventilatory support.
2. A GCS score ≤ 10 was significantly associated with an increased need of ventilatory support.
3. Greater time lag between consumption of poison and admission to hospital (≥ 4 hours) was associated with higher need for ventilator support.
4. Higher respiratory rate (> 25 breaths/minute) and accessory muscles of respiration in action was significantly associated with higher need for ventilator support.
5. O₂ saturation of ≤ 89 mmHg was significantly associated with higher need for ventilatory support.
6. Grade 3 severity of poisoning was associated with higher need for ventilator support.
7. Dose of atropine greater than 150 mg within 48 hours of admission was associated with higher need for ventilatory support.
8. The relationship between age group and sex with ventilatory support was not found to be significant.
9. Size of the pupil and pulse rate, type of organophosphorus compound consumed had no relevance in predicting the need for ventilatory support.

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