Original Paper

Management of Organophosphorus Compound Poisoning - A One Year Experience in a Tertiary Care Hospital

Vaidyanathan R*, Ashoka HG**, Pramod Kumar GN***

ABSTRACT

This study was undertaken to assess the distribution pattern, outcome and possible predictors affecting the mortality and the need for ventilator support in patients who had consumed organophosphorus compound pesticides. 91 patients who were admitted to the ICU between April 2009 and March 2010 with history of ingestion of organophosphorus pesticide, were studied. Baseline clinical assessment and investigations were undertaken and SOFA and APACHE II scores were calculated.

Out of 91 patients, 39 required ventilator support. Of these 39 patients, 2 died, one due to severe sepsis and multiorgan dysfunction, and the other, a chronic alcoholic with chronic liver disease, due to hepatic encephalopathy and multiorgan dysfunction. The time elapsed since ingestion of poison, SOFA and APACHE II scores were significantly associated with patients requiring ventilator support. However with logistic regression analysis, none of these variables were able to either predict mortality or the need for ventilator support.

The overall outcome in these cases was favourable as the mortality rate was 2.3%. Though the time elapsed since ingestion of the pesticide and the APACHE II score were found to predict the need for ventilation in many earlier studies, they failed to predict either the need for ventilation or mortality in the present study. The improved mortality rate could be attributed to an organized approach through protocols between the emergency department and the ICU in order to successfully manage patients with organophosphorus compound poisoning.

Key Words: Organophosphorus compound (OPC); Pesticide; Mechanical ventilation; APACHE II; SOFA

Introduction

Organophosphorous compound poisoning is a major health problem not only in the developing countries but also in Western countries.[1] Hospital-based statistics suggest that nearly half of the admissions to the emergency department with acute poisoning are due to organophosphorus compound (OPC) poisoning.[2]

Organophosphorus compound poisonings are a leading cause of death in agrarian countries all over the world.[3,4] These compounds were first discovered more than 100 years ago, and are at present the predominant group of pesticides employed globally for pest control.[5] OPC poisoning affects approximately a population of 3 million and causes 2,00,000 deaths annually with most of these occurring in developing countries.

The diagnosis of OPC poisoning is based on the history of exposure and features of cholinergic overactivity.[6] The early causes of death 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.[7] Late mortality is associated with respiratory failure and infections such as pneumonia, septicaemia, or complications related to mechanical ventilatory support and intensive care management.[8-10] Medical management is difficult,

*Consultant Anaesthesiologist & Intensivist, Cauvery Hospital, Teresian Circle, Siddharthanagar, Mysore 570001, Karnataka
**Dept. of Medicine, JSS Medical College Hospital, JSS University, Mysore 570004, Karnataka
***(*Author for correspondence*): Dept. of Forensic Medicine & Toxicology, JSS Medical College, JSS University, Mysore 570015, Karnataka. Email: drpramodkumargn@gmail.com

with case fatality often over 20%.[11] Improved medical management of OPC poisoning will result in a marked reduction in the global number of deaths from suicide.

Early resuscitation with atropine, oxygen, respiratory support, and fluids is required to improve oxygenation of patients. The role of oximes is unclear; they may only benefit patients poisoned by some compounds, or patients with moderate poisoning. Small studies have suggested possible benefit from new treatments like magnesium sulfate and clonidine, but much larger trials are needed. RCTs are now underway in rural Asia to address particular aspects of therapy.[11] However, some specific OPC pesticides may ultimately prove very difficult to treat with current treatment regimens, and focused bans may be the only method to substantially bring down the case fatality for OPC pesticide poisoning.

This study was carried out to investigate the pattern and distribution of OPC poisoning in a tertiary care hospital, and also to discover any possible predictors of mortality, and factors which might predict the need for ventilator support.

Materials and Methods

Ninety one patients who were admitted with history of ingestion of organophosphorus compound (OPC) pesticide to the ICU from March 2009 to April 2010 were included in this study. All patients received thorough skin decontamination and stomach wash in the emergency room (ER). Atropine was started at a rate of 0.2mg/kg/hr and was later titrated to the desired effects. Pralidoxime (PAM) was given 1gm IV twice a day for 3 days. All patients also received inj. ceftriaxone, 1g IV twice a day. Airway was secured for those patients who needed it and ventilator support was initiated as indicated. Baseline clinical assessment, investigations, APACHE II and SOFA scoring were done on all patients. Other variables which were evaluated included age, serum cholinesterase levels, type of the compound consumed, time elapsed since ingestion of poison, and the presence or absence of any culture-proven infections.

Statistical Analysis: SPSS for Windows Version 11.5 was used for statistical analysis. Parameters significant on univariate analysis ($P<0.05$) were identified as potential predictors for the need of mechanical ventilation, and were further evaluated using multivariate logistic regression analysis, with the clinical outcome and requirement of ventilatory support as the dependent variable.

Results

The majority of the patients in the study group were males (M:F=73:18), the mean age being 30 +/-10**.**The youngest was a 6-year school boy who had accidentally consumed an OPC pesticide, while the oldest was an 85-year old male with chronic obstructive pulmonary disease (COPD). The overall rate of admission of OPC poisoning to the ICU was approximately 12% (11.52%) though the total percentage of patients requiring ventilatory support due to OPC ingestion was 30.95%**.**

Dimethoate was the commonest OPC consumed (35% cases), followed by quinalphos and chlorpyriphos (14% each) **(Table 1)**. In 16 patients, the exact compound could not be identified, and the diagnosis was based on history of ingestion, characteristic odour, and signs and symptoms of cholinergic overactivity. Out of the 91 patients, 39 required ventilator support, and 2 patients died while on ventilator support bringing the overall mortality rate to 2.1%. One patient who was a chronic alcoholic was suffering from chronic liver disease. He developed nosocomial infections and died due to multiorgan dysfunction. The second patient had severe aspiration pneumonia - sepsis - ARDS.

Table 1 Percentage Distribution of Pesticides in the Study

Type of Pesticide	No of Patients	Percentage
Dimethoate	32	35.16%
Quinalfos	13	14.29%
Chlorpyriphos	13	14.29%
Methyl Parathion	9	9.89%
Carbamate	3	3.30%
Endosulfan	3	3.30%
Cypermethrin	1	1.10%
Monocrotophos	1	1.10%
Unknown	16	17.58%

Four of these 39 patients were brought to us already intubated. The mean duration of mechanical ventilation was 7 days (maximum 21 days), and the mean duration of ICU stay was 6 days. The mean serum cholinesterase level was 2100 (2198 for patients on ventilatory support and 3443 for patients not on ventilatory support)

(**Table 2)**. Serum cholinesterase was not significantly associated with either the mortality or the patients requiring ventilator support. Five of these patients required tracheostomy in the ICU. Four patients developed VAP, though all of them recovered; one developed severe sepsis. Culture-proven infections were seen in 8 patients. The commonest organism isolated was *Staphylococcus aureus* which was isolated from 4 patients. Other organisms grown included *Pseudomonas* in 2 patients, and *Klebsiella* in another 2 patients. One patient had UTI with *Klebsiella*. All these patients recovered with appropriate antibiotics.

Four patients developed ARDS. One of them had myoglobulinuria and acute pancreatitis. He responded favourably, and completely recovered after 14 days of ventilator support. One patient died during the course of treatment, while the other two recovered without any further complications. One patient had severe viral myocarditis. Five patients had severe anaemia and 3 of them required transfusions. All but one of them had microcytic hypochromic anaemia indicating nutritional deficiency, while the other one had dimorphic anaemia.

Five patients in our series were chronic alcoholics. One of them presented with severe delirium tremens. While one of these patients who had chronic liver disease died of nosocomial infection and multiorgan dysfunction, all the others recovered. Five out of the 39 patients had COPD. The oldest among them was an 85-year old male. All of them made good recovery with the mean duration of ventilation being 9.2 days. NIV was used during weaning in 3 of them. Other complications included upper GI bleed which was seen in one patient, and coagulopathy which was seen in another.

Three pregnant women were admitted with history of ingestion of OPC pesticide. Two of them required ventilator support. One delivered a healthy baby, while the other had to undergo induced abortion.

The mean APACHE II score was 9.9, and that for patients requiring ventilator support was 13. The mean SOFA score was 1.2, and was 1.6 for patients requiring ventilator support. The time elapsed since consumption of the compound (0.032**)** SOFA score (0.006**)** and APACHE II score (0.005**)** were significantly associated with the need for mechanical ventilation with p value less than 0.05 **(Table 2).**

These 3 variables, namely the time elapsed since ingestion of the compound, SOFA score and APACHE II score were further analysed using logistic regression analysis, and none of them independently predicted the need for ventilator support, and neither did the serum cholinesterase levels **(Table 3).**

Similarly none of these potential variables such as age of the patient, type of the poison, time elapsed since ingestion, SOFA score, APACHE II score, presence of infection, or the duration of mechanical ventilation were significantly associated with mortality.

Discussion

OPC pesticide poisoning is one of the most common causes requiring ICU admissions and ventilator support in our country. An estimated 12% of all ICU admissions have been shown to be due to OPC ingestion, and 30% of the patients who require ventilator support are victims of OPC exposure. More than 70% of all admissions due to poisonings are due to OPCs.[12,13] In contrast to the

Table 2 Comparison of Patients Requiring Ventilator Support v/s Not Requiring Ventilator Support

Variable	Overall Mean	Patients on Ventilator (Mean)	Patients not on Ventilator (Mean)	p Value
Time since ingestion (hrs)	9.14	8.1	5.41	0.032
Serum cholinesterase level	3865.63	2181.47	3443.71	0.08
No of ICU days	6.5	8.64	4.29	0.000
SOFA	1.31	1.84	1.01	0.006
APACHE II	10.11	11.41	8.96	0.005

Table 3 Logistic Regression Analysis Results

Variable	Odds Ratio	95% CI	'p' Value
Time	3.493	5.37 – 7.86	0.062
SOFA	0.975	1.07 – 1.67	0.323
APACHE II	3.413	9.14 – 10.90	0.065

Indian scenario of suicidal exposures, the majority of the cases reported in Western literature is due to either accidental consumption or due to chemical warfare or terrorist attacks, as was seen in the Tokyo subway attacks.[14]

In the present study, 11.72% of the ICU admissions were due to OPC poisoning, and 31.8% of patients requiring ventilator support were victims of OPC exposure, similar to what has been reported by Cherian et al.[13]

A male preponderance was noted in this study with the majority of them falling in the economically most productive age group of 25-40 years, as has been consistently shown in many earlier studies.

Various grading methods are available to help in assessing the severity, and effectively manage OPC poisoning. However it has been found that this always does not correlate with the outcome, as patients who appear to recover in the first 24-48 hours, later develop intermediate syndrome. Ingestion of dimethoate and methyl parathion has been shown to be associated with more severe forms of poisoning often requiring ventilator support in more than 50% of such cases.[14] In our study, the commonest OPC has been dimethoate accounting for 35% of the cases, followed by methyl parathion, chlorpyriphos, a carbamate compound, and endosulfan, each amounting to around 12%. In another 12% of the patients, the exact nature of the compound was not known. In this study, the nature of the compound was not significantly associated with either the need for mechanical ventilation or mortality.

The mean time elapsed since the ingestion of poison up to the time of admission in our study was 6 hours. It was 8.2 hours for patients requiring ventilator support and was significantly associated with patients requiring ventilator support. The mean SOFA score was 1.02, whereas for patients requiring ventilator support it was 1.64. The mean APACHE II score was 9.9, and that for patients requiring ventilator support it was 11.8.

These three parameters along with the serum cholinesterase levels were analyzed using logistic regression analysis, and none of them were found to independently predict either the need for ventilator support, nor the mortality.

Various parameters like APACHE II, GCS on admission, time elapsed since ingestion of the poison, duration of mechanical ventilation and presence of infections have been associated with mortality and independently shown to predict mortality.[14-17] However, none of these parameters were shown to independently predict mortality in our study, except GCS as an independent variable in the study.

Similarly APACHE II, SOFA score, SAPS score, type of poison consumed (dimethoate and methyl parathion over others) and time elapsed since ingestion of poison have been shown to predict the need for mechanical ventilation.[13-15] None of these parameters were shown to predict the need for mechanical ventilation in our study.

The overall mortality in patients consuming OPCs range from 8%-50%.[18-20] The commonest causes of mortality have been identified as delay in initiating timely care, hospital acquired infections and other complications associated with ventilator support.[14]

Special situations: While treating patients with OPC poisoning, especially those requiring ventilator support, one may come across special subgroups of patients such as paediatric patients as was the case in our series. Pregnant patients who have ingested OPC insecticides during the second or third trimester of pregnancy have been successfully treated with atropine and pralidoxime, and later delivered healthy newborns with no significant abnormalities. However, foetal distress is a possibility both due to poisoning and its treatment.[21] Pregnant women should receive the same treatment as that given to other adults.[22] Both atropine and pralidoxime are pregnancy class C drugs.

In our study, 3 pregnant patients got admitted with ingestion of OPC compound. Two of them were put on the ventilator. One delivered a healthy baby, while the other had to undergo induced abortion. In the Tokyo subway attacks, 5 pregnant women had mild poisoning and all had normal babies without complications.[14]

Other co-existing medical diseases which can alter the management of the patients in the ICU especially those on ventilator should be kept in mind and accordingly managed. In the present series patients with co-existing medical diseases like COPD, anaemia, and chronic liver disease had a favourable response and were accordingly managed.

Acknowledgements

The authors would like to acknowledge the help of Dr Annie J Verghese, Associate Professor of Forensic Medicine & Toxicology, in editing and proof reading the manuscript. This study was presented by the first author in the State Conference of Indian Society of Anaesthesiologists, Karnataka Chapter, at Kolar (27th August 2010), Karnataka, India.

REFERENCES

1. Peter JV, Cherian AM. Organic insecticides. *Anaesth Intensive Care* 2000;28(1):11–21.
2. Singh S, Sharma N. Neurological syndromes following organophosphate poisoning. *Neurology India* 2000;48(4):308–313.
3. Singh S, Wig N, Chaudhary D, Sood NK, Sharma BK. Changing pattern of acute poisoning in adults: Experience of a large North-West Indian Hospital (1970- 1989). *J Assoc Physicians India* 1997;45:194–197.
4. Malik GM, Mubarik M, Romshoo GJ: Organophosphorus poisoning in the Kashmir valley, 1994 to 1997. *N Engl J Med* 1998: 9; 338(15):1078.
5. Koelle GB. Pharmacology and toxicology of organophosphorous and carbamates. In: Ballantyne B, Marrs T (editors). Clinical and Experimental Toxicology of Organophosphates and Carbamates. 1992. Oxford, Butterworth Heinemann. 33-37.
6. Namba T, Nolte CT, Jackrel J, Grob D. Poisoning due to organophosphorous insecticide. *Amer J Med* 1971;50:475–479.
7. Steward WC, Anderson EA. Effects of cholinesterase inhibition when injected into the medulla of the rabbit. *J Pharmacol Exp Ther* 1968;162:309–318.
8. Tsao TC, Jwang Y, Lan R, Sheieh W, Lee C. Respiratory failure in acute organophosphorous and carbamate poisoning. *Chest* 1990;98:631–636.
9. Bardin PG, Van Eeden SF, Joubert JR. Intensive care management of acute organophosphorus compound: A 7-year experience in the West Cape. *South Afr Med J* 1987;72:593–597.
10. Bardin PG, Van Eeden SF. Organophosphorus poisoning: Grading the severity and comparing treatment between atropine and glycopyrolate. *Crit Care Med* 1990;18:956–960.
11. Eddleston M, Juszczak E, Buckley NA, Senarathna L, Mohamed F, Dissanayake W, et al. Multiple-dose activated charcoal in acute self-poisoning: A randomised controlled trial for the Ox-Col Poisoning Study collaborators. *Lancet* 2008;371(9612):597–607.
12. Davies JE. Changing profile of pesticide poisoning. *N Engl J Med* 1987;316:807–808.
13. Cherian MA, Roshini C, Peter JV, Cherian AM. Oximes in organophosphorus poisoning. *Indian J Crit Care Med* 2005;9(3): 155–163.
14. Okumura T, Takasu N, Ishimatsu S, Miyanoki S, Mitsuhashi A, Kumada K, et al. Report on 640 victims of the Tokyo subway sarin attack. *Ann Emerg Med* 1996;28(2):129–135.
15. Goel A, Joseph S, Dutta TK. Organophosphate poisoning: Predicting the need for ventilatory support. *J Assoc of Phys India* 1998;46:786–790.
16. Eun-Jung K, Su-Jin S, Kwon-Hyun L, Hyo-Wook G, Jong-Oh Y, Eun-Young L, Sae-Yong H. Factors for determining survival in acute organophosphate poisoning. *Korean J Intern Med* 2009; 24(4):362–367.
17. Davies J, Eddleston M, Buckley NA. Predicting outcome in acute organophosphorus poisoning with a poison severity score or the Glasgow coma scale. *QJ Med* 2008;101(5):371–379.
18. Kumar SS, Jayarajan A, Kuppaswamy G. Continuous infusion of high dose of atropine in management of organophosphorus poisoning. *J Assoc Phys India* 1991;39:190–193.
19. Wadia RS. Treatment of organophosphate poisoning. *Indian J Crit Care Med* 2003;7(2): 85.
20. Cherian AM, Peter JV, Johnson S, et al. Effectiveness of oximes (PAM - Pralidoxime) in the treatment of organophosphorus poisoning (OPP): A randomized, double-blind placebo controlled clinical trial. *J Assoc Phys India* 1997;45:22–24.
21. Paudyal BP. Organophosphorus poisoning. J Nepal Med.Assoc 2008; 47(172): 251-258.
22. Munidasa ADD, Gawarammana IB, Kularatne SAM, Kumarasiri PVR, Goonasekera CDA. Survival pattern in patients with acute organophosphate poisoning receiving intensive care. *Clinical Toxicol* 2004;42(4):343–347.