

Pralidoxime Treatment and Serum Cholinesterase Levels as Predictor of Outcome in patients of Acute Organophosphate Poisoning

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ABSTRACT:

Objective: To compare the outcome of acute organophosphate poisoning with and without Pralidoxime treatment.

Methods: It is a retrospective study conducted at the Department of Medicine, Department of Paediatric Medicine and Department of Pathology Bahawal Victoria Hospital Bahawalpur from July 2009 to June 2010. It included 241 patients of acute OP poisoning. Blood urea, serum creatinine and cholinesterase levels were done. One hundred and ninety six patients were given Pralidoxime with Atropine and remaining 45 were treated with Atropine alone. Data was analyzed using SPSS 17. P value of <0.05 was taken as significant.

Results: Majority of patients (60.6%) were between 21-30 years of age. Male to female ratio was 2:1. Out of total, 17(7.0%) patients died. Shorter time interval from the onset of OP poisoning to the start of treatment ($p = 0.000$) and the use of Pralidoxime therapy (0.001) were associated with better patient survival. Three out of 13 patients admitted in ICU died, all having low serum cholinesterase levels

Conclusion: It is observed that use of Pralidoxime increases the patient survival significantly in acute organophosphate poisoning and low serum cholinesterase has poor prognosis.

Key words: Serum cholinesterase, Pralidoxime, acute organophosphate poisoning.

INTRODUCTION

Organophosphate compounds (OPCs) comprise a wide range of chemicals which are used as insecticides, herbicides, fungicides and others. These are used worldwide in agriculture¹. Use of pesticides has increased food production in parallel with the population growth in many parts of the world. In some countries they are used as chemical agents of warfare. OPCs may cause acute or chronic poisonings after accidental or suicidal exposure. It is the commonest suicidal agent in the developing countries like Pakistan. Toxicity generally results from accidental, intentional ingestion or from exposure to agricultural pesticides.^{2,3} Early diagnosis and appropriate treatment with atropine with or without oximes is often life saving^{4,5}. The clinical course of OP poisoning may be quite severe and may need intensive care management^{6,7,8}. The current study is conducted to compare the patient outcome with and without Pralidoxime therapy in cases of acute organophosphate poisoning. Low serum cholinesterase levels at the beginning of therapy is associated with poor prognosis^{9,10}. Low Glasgow Coma Score during stay in the hospital is also indicator of bad prognosis^{11,12}.

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PATIENTS AND METHODS

The retrospective data of patients of OP poisoning between July 2009 and June 2010 was retrieved from the charts of patients. The diagnosis of OP poisoning was based on history of exposure and clinical manifestations of OP poisoning including excessive salivation, miosis, diarrhoea, bronchorrhoea, bronchospasm, bradycardia, muscle weakness and urination. The patients exposed to other poisons were excluded. All patients received standard medical treatment under the direction of the hospitals' consultant physicians. Patients of OP poisoning divided in to two groups. Group A included those patients who were given rapid atropinization, with doubling doses of atropine at 5–10 min intervals, starting at 1–3mg, given until muscarinic signs were abolished. Group B included those patients who received pralidoxime chloride 1g IV four times a day for 1–3 days along with rapid atropinization. Data was transferred on the structured Performa including demographic characteristics, clinical presentation, laboratory test (complete blood counts, blood urea, serum creatinine, serum cholinesterase levels) and outcome. Data was analyzed using SPSS-17. Frequencies and percentages were computed for qualitative data like sex and marital status. Chi square was applied to determine statistical significance. P value <0.05 was considered significant.

RESULTS

Most of the patients (n=166/241, 69%) belonged to age group of 15-25 years as shown in Figure-1. Regarding gender distribution, a male predominance (n=158, 65.6%) was observed. Calculated male to female ratio was 2:1. About half of the patients (n=134, 55.6%) were married and remaining were unmarried.

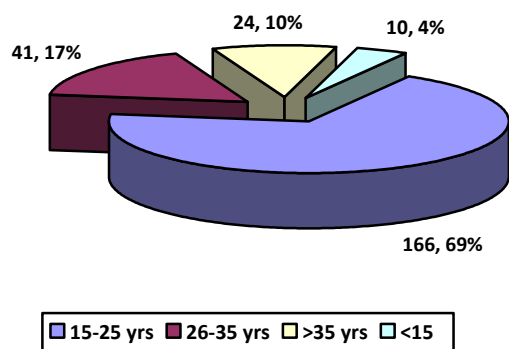


Fig1: Age distribution of patients presenting with OP poisoning

Majority of patients (n=157, 65.1%) were brought to hospital within first three hours of the exposure to organophosphates. Based on time of arrival, patients were divided into two groups. Group-1 included those who reached within six hours from the time of exposure. They were 196 patients (81.3% of the total) and were treated with combined therapy (pralidoxime and atropine). Group-2 included 41 patients who presented later than six hours and were treated with atropine alone. Table-1 shows the comparison of outcome on basis on time of arrival which affects the outcome significantly ($p = 0.0001$).

Table 1: Time of arrival and outcome of OP poisoning (n=241)

Time	Recovery	Death	Total	%age
< 6 hours	194	6	200	3
> 6 hours	30	11	41	26.8
Total	224	17	241	7.0

P value = 0.0001 df=2

Patients who received pralidoxime and atropine therapy showed excellent outcome by a recovery rate of 97.45% and death rate of 2.55% as compared to patients who received atropine therapy alone had a recovery rate of 73.4% and a death rate of 26.6% as shown in Table-2 which is statistically significant ($p = 0.0001$)

Table 2: Comparison of outcome on basis of treatment (n=241)

Therapy	Recovery	Death	Total	%age
Atropine+ Pralidoxime	191	5	196	2.55
Atropine only	33	12	45	26.6
Total	224	17	241	7.0

P value = 0.0001 df=1

Thirteen patients were admitted in ICU, serum cholinesterase level was done in these patients. Four patients had low serum cholinesterase levels. Total 3 out of 13 patients admitted in ICU died. All deceased patients had low serum cholinesterase levels. Glasgow Coma Score (GCS) was < 7 in all deceased patients.

Table 3: Association of serum cholinesterase levels with mortality in ICU patients (n=13)

	Total	Deceased	%age
Low serum cholinesterase	4	3	75
High serum cholinesterase	9	0	0
Total	13	3	23.1

P value: 0.014, df:1

DISCUSSION

The primary mechanism of action of organophosphates is inhibition of acetyl cholinesterase. Organophosphates inactivate acetyl cholinesterase by phosphorylating the serine hydroxyl group located at its active site. They inhibit both red blood cell acetyl cholinesterase and pseudocholinesterase (plasma cholinesterase) activity. The inhibition of acetylcholinesterase causes accumulation of acetylcholine at synapses with resultant central and peripheral nervous systems. After some time the acetylcholinesterase organophosphorous compound undergoes a conformational change that make the enzyme irreversibly resistant to reactivation by an antidote¹⁶. The clinical features of OP poisoning are due to excess acetylcholine at the muscarinic and nicotinic receptors. Symptoms of cholinergic crisis are due to stimulation of the muscarinic and nicotinic receptors: Nicotinic manifestations include increased or decreased muscle power and skeletal muscle fasciculations. Muscarinic manifestations include excessive salivation, miosis, diarrhea, bronchorrhoea, bronchospasm, bradycardia and urination.

OP poisoning is a serious problem in agricultural areas. It has high morbidity and mortality. Mortality is 6-24 % in different part of the world^{13,14}. Mortality in our study is also 7.0%. Outcome in the patients of OP

poisoning depends upon various factors such as type of OP poison¹⁷, amount of poison ingested, duration between exposure and arrival in the hospital, treatment with or without oxime, Glasgow Coma Scale. Low serum cholinesterase levels is poor prognostic indicator of outcome^{18,19}.

In our study outcome was good in patients who reached hospital within six hours than those patients who came after six hours. The outcome was also good in those patients whom oximes were given than atropine group only. Low serum cholinesterase levels in ICU patients of OP poisoning were associated with high mortality.

CONCLUSION

It is observed that use of Pralidoxime increases the patient survival significantly in acute organophosphate poisoning. So all the patients reaching in the hospital within six hours of exposure of OP compounds should receive pralidoxime along with atropine. Low serum cholinesterase levels at the time of admission in hospital is indicator of poor prognosis.

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