Original article:

Prognostic value of clinical and lab parameters in assessing the severity of organophosphorous compound poisoning

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Abstract

Introduction: Respiratory failure is the most common complication of OP poisoning leading to death. Owing to limited availability of resources in India, it is important that clinical features and criteria to predict the need for ventilator support be identified at initial examination. Our aim was to assess the severity of organophosphorus compound poisoning clinically by using Peradeniya scoring and by estimating serum cholinesterase and serum amylase levels. Severity will be predicted in terms of need for ventilator support and dose of atropine needed.

Methods: This was an observational study done at H.S.K hospital, a teritary care center at Bagalkot. 60 patients fulfilled inclusion criteria, were included in the study.

Results: In this study need for ventilator support was seen in 26.6% of patients. 62.5% of patients with moderate poisoning and 100% of patients with severe poisoning according to POP scale required ventilator support. Serum cholinesterase levels and serum amylase levels also correlated well with need for ventilator support(p value<0.05).Mean dose of atropine required was high in patients with low pche levels(442.67mg), high serum amylase levels(260.33mg) and severe grade on POP scale(584mg) when compared to patients with normal pche levels(72.76mg), amylase levels(86.81), mild grade on POP scale(86.76mg) respectively.

Conclusion: Peradeniya OP poisoning scale, serum cholinesterase levels, serum amylase levels all correlated well with severity of poisoning particularly in terms of need for ventilator support and dose of atropine required.

Key words: peradeniya op poisoning scale, serum amylase levels, serum cholinesterase levels, ventilator support, atropine.

Introduction

It is estimated by World Health Organization (WHO) that around 0.3 million people die every year globally due to various poisonings¹.A Recent study from south India reported mortality rate of 4% in poisoning cases². OP compounds are used as pesticides, herbicides, chemical warfare agents in form of nerve gases³. WHO estimates that pesticide poisonings causes more than 2,20,000 deaths in

developing countries like India⁴. Because of their easy availability, organophosphorus (OP) compounds are commonly used for suicide⁵.Organophosphorus (OP) compounds inhibit acetyl cholinesterase and butyryl cholinesterase enzymes resulting in over stimulation at cholinergic synapses ⁶. The definitive and the gold standard method in the diagnosis of OPC poisoning is established by demonstrating a decreased cholinesterase in the blood^{7,8}. Peradeniya OP poisoning scale has not been studied much in Indian scenario it could be a simple and effective system to determine the need for ventilator support early on in the course.

Elevated serum amylase (hyperamylasemia) secondary to pancreatic injury because of parasympathetic overstimulation and hypersecretion has been noted in human beings. Studies have shown that serum amylase above the normal range on the day of admission was related to the development of respiratory failure and the elevation of amylase level and predictive of subsequent respiratory failure⁹. This study may help in predicting clinical outcome and in making timely decisions regarding shifting patients to ICU. Our objectives were to find out the prognostic significance of Peradeniya OP poisoning scale, serum cholinesterase and serum amylase levels in predicting the severity of OP poisoning predicted in terms of need for mechanical ventilation and total dose of atropine needed.

Materials and methods

Study design: An observational study.

Study period: January 2013 to December 2013.

Inclusion criteria: A history of exposure to organophosphorus compound within previous 24 hours as indicated by patient or relatives or the referring doctor, with characteristic clinical manifestations of organophosphorus compound poison and physical evidence of the poison consumed.

Exclusion criteria:

- Patients with concomitant illness or conditions that are likely to alter the respiratory effort due to organophosphorous compound poisoning.
- Patients who consumed other poisons along with organophosphorus compound.

- 3. Patients with chronic lung disease
- 4. Patients treated outside for the poisoning

5. Patients who have consumed poison along with alcohol

- 6. Patients who were chronic alcoholics
- 7. Patients with a history of pancreatitis will be excluded from the study.

The Ethical committee approval was obtained to carry out the study in the hospital.

Patients of OP poisoning admitted in S.Nijaligappa medical college hospital were studied. Information was collected through a preformed and pre-tested proforma from each patient. Qualifying patients were subjected for a detailed history, clinical examination and relevant biochemical investigations. A thorough clinical examination was carried out with particular reference to vital parameters, pupil size, assessment of central nervous system, respiratory system, cardiovascular system as per prescribed proforma. This examination took place during initial presentation and the cases were followed up during treatment of the patient. Peradeniya OP poisoning scale was applied to all study subjects and the severity of OP poisoning was graded as mild, moderate, severe at the time of admission.

In all study subjects, 3 ml of plain blood was collected on admission before administration of atropine, plasma cholinesterase and serum amylase were estimated. Apart from serum amylase and serum cholinesterase other relevant and routine investigations were done as per need.

According to cholinesterase activity the organophosphorus poisoning was graded as¹⁰:

The normal values ranged from 2710-11,510U/L at 37 C.

Reference range for serum α -amylase activity is 20-88U/L.

Data was tabulated in Microsoft excel and later SPSS software and OPEN EPI version 2.3.1 was used for analysis of data. Student 't' test was used to analyse quantitative data and Pearsons Chi square test was used to analyse qualitative data. By using the above mentioned tests, test of significance was calculated. A 'p' value less than 0.05 is statistically significant.

Peradeniya op poisoning scale

Sl.no	Parameter	Score
1	Miosis-	
	Pupil > 2mm	0
	$Pupil \leq 2mm$	1
	Pupils pin point	2
2	Fasciculations-	
	none	0
	Present but not generalized or continuous	1
	Generalised and continuous with central cyanosis	2
3	Respiration –	
	Respiratory rate ≤ 20 /min	0
	Respiratory rate > 20/min	1
	Respiratory rate > 20/min with central cyanosis	2
4	Bradycardia –	
	Pulse rate > 60/min	0
	Pulse rate 41-60/min	1
	Pulse rate \leq 60/min	2
5	Level of consciousness –	
	Conscious and rational	0
	Impaired, responds to verbal commands	1
	Impaired, no response to verbal commands (if convulsion	2
	present add 1)	
	Total	11

Results:

The results of this study which included 60 patients were as follows

Table no 1	: Distribution	of patients	according to age
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Age Group (in years)	No. of patients	Percentage
<20	7	11.7
21 - 30	33	55
31 - 40	15	25
41 - 50	4	6.7
51 -60	1	1.6
Total	60	100

Age group ranged from 17 years to 52 years. Majority of the patients were in the age group of 21-30 years which comprised 55% of the study patient

Gender	No. of patients	Percentage	
Male	32	53.3	
Female	28	46.7	
Total	60	100	

Table no: 2 Distribution according to gender

In this study, 32 (53.3%) of patients were males and 28 (46.7%) of the cases were females.

Table no: 3 Distribution according to place of residence

Place	Male	Female	Total
Rural	26	20	46(76.6%)
Urban	6	8	14(23.4%)

76.6% of the patients in the present study are from rural area and rest 23.4% of the patients were from urban area.

Mode of poisoning	No. of patients	Percentage
Suicidal	58	96.7
Accidental	1	1.7
Homicidal	1	1.7
Total	60	100

Table no: 4 shows distribution of patients according to intention of poisoning

58 (96.7%) patients consumed poison with suicidal intention .only 1 patient consumed accidentally and 1 patient homicidally.

Type of OP compound	No. of patients	Percentage
Endosulphan	10	16.7
Malathion	15	25
Monocrotofos	3	5
Parathion	9	15
Dimethoate	6	10
Fenetrothion	3	5
Metapar	4	6.7
Chlorpyrifos	6	10
Quinolfos	1	1.7
Dichlorfos	3	5
Total	60	100

 Table no: 5 Shows type of poison consumed by the patients

Malathion is the most common poison consumed in this study by 25% of the patients followed by Endosulphan (16.7%) and parathion (15%).

Symptoms	No. of patients	Percentage
Bronchorrhea	26	43.3
Salivation	37	61.7
Sweating	36	60
Lacrimation	27	45
Breathlessness	16	26.7
Nausea	55	91.7
Vomiting	45	75
Diarrhoea	20	33.3

Table no: 6 shows presenting symptoms

The Most common symptom reported by patients in this study was nausea (91.7%) followed by vomiting (75%). Increased salivation was reported by 61.7% of patients and sweating by 60% of patients.

Table no: 7 Shows clinical signs at presentation

Signs	No. of patients	Percentage
Miosis	23	38.3
Fasiculations	40	66.7
Bradycardia	16	26.7
Tachypnoea (RR>20/min)	36	60
Altered consciousness	10	16.7
Convulsions	4	6.7

In our study the most commonly found clinical sign was fasciculations in 66.7% of patients followed by tachypnea in 60% of patients.

Peradeniya op p	ooisoning scale	No. of patients	Total
Mild	0	11(18.3)	42(70)
	1	9(15)	
-	2	8(13.3)	
-	3	14(23.3)	
Moderate	4	6(10)	16(26.7)
-	5	3(5)	
_	6	3(5)	
-	7	4(6.7)	
Severe	8	2(3.3)	2(3.3)
-	9-11	0	

Table no: 8	Shows	severity	of	poisoning	according	to pop	p scale
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Table no: 9 association between individual parameters of peradeniya op poisoning scale with need for ventilator support

parameter	Score	Ventilator support		Total	Significance	
		YES	NO		X ²	P value
Miosis	0	0	22(100)	22	24.990	.0001
	1	5(21.7)	18(78.3)	23		
	2	11(73)	4(27)	15		
Fasciculations	0	0	15(100)	15	19.219	.0001
	1	11(27.5)	29(72.5)	40		
	2	5(100)	0	5		
Respiratory	0	1(4)	23(96)	24	10.355	.001

Numbers in parenthesis indicates percentage

In this study 70% of the patients belonged to mild grade (0-3). 26.7% of the patients belonged to moderate grade (4-7) and only 3.3% of patients belonged to severe grade(8-11).

rate	1	15(41.6)	21(58.4)	36		
	2	0	0	0	-	
Bradycardia	0	5(11.3)	39(88.4)	44	19.759	.0001
	1	11(68.7)	15(31.3)	16	_	
	2	0	0	0		
Consciousness	0	79(14)	43(86)	50	24.614	.0001
	1	9(90)	1(10)	10		
	2	0	0	0		
Convulsions	0	12(21.5)	44(78.5)	56	11.786	.001
	1	4(100)	0	4		

P value was significant for all the parameters in the above table. In the above table comparisons of individual components of POP scale in predicting the need for ventilator support was shown. In patients with miosis of 1mm 21.7 % required ventilator support. Among patients with pinpoint pupil 73% required ventilator support. This was statistically significant. In patients with fasiculations 27.5% of patients with score 1 required ventilation and 100% of the patients with generalized fasiculations required ventilator support. This association was statistically significant. Respiratory rate scoring was statistically highly significant. 41.6% of patients with respiratory score of 1 required ventilator support.68.7% patients who had a POP score of 1 for bradycardia required ventilator support.

Table no: 10 shows association between pop scale and need for ventilator support

Severity of poisoning	Ventilato	Total no. of patients	
	Yes	No	
Mild	4(9.5)	38(90.5)	42
Moderate	10(62.5)	6(37.5)	16
Severe	2(100)	0	2

Numbers in parenthesis indicate percentage.

Chi square test-22.317

p value-0.001 highly s

Only 9.5% of patients with mild grade of poisoning according to POP scale required ventilator support, where as 90.5% did not require ventilator support. Most of patients with moderate (62.5%) and severe

poisoning (100%) according to POP scale required ventilator support. This was statistically highly significant.(P value -0.001).

Pseudo cholineterase	ventilato	Total	
levels	Yes	No	_
Normal	0	26(100)	26
20-50%	12(40)	18(60)	30
10-20%	3(100)	0	3
Less than 10%	1(100)	0	1
Total	16	44	60

Numbers in parenthesis indicate percentage

Chi-square test- 23.182 p value- 0.001 highly significant

100% of patients with normal grade of poisoning did not require ventilator support.

Total	or support	Serum amylase Levels in u/l	
	No	Yes	_
42	38(90.5)	4(9.5)	<88u/l
18	6(33.3)	12(66.7)	>88u/l
60	44	16	Total
	44	16	Total

Table no:	12 shows	association	between serum	amylase	levels and	need for	ventilator	support

Numbers in parenthesis indicate percentage

Chi-square test-21.039 p value-0.001 Highly significant

^{90.5%} of patients with normal serum amylase levels did not required ventilator support whereas 66.7% of the patients with elevated serum amylase levels required ventilator support. P value was highly significant for this association.

POP scale	Total dose of atropine needed		
	Mean	Standard deviation	
Mild	86.76	45.89	
Moderate	220.00	138.35	
Severe	584.00	684.47	

Table no: 13 showing association between pop scale and dose of atropine needed

P value is significant between mild and moderate group (p value-0.001) as well as moderate and severe group. (p value-0.04)

Mean dose of atropine required for patients with mild pop scoring is 86.76 mg whereas in severe group it is 584 mg. This association was statistically significant.

Table no: 14 shows association between serum cholinesterase and mean dose of atropine needed

Pseudo cholinesterase	Mean dose of atropine needed in mg			
levels	Mean	standard deviation		
>50% (26)	72.69	27.029		
20-50%(30)	162.80	122.444		
10-20%(3)	442.67	542.385		
<10%(1)	230.00	-		

Numbers in parenthesis indicates no. of patients.

Mean dose of atropine needed in patients with pche levels >50% is 72.69 mg and it was 442.67 mg in patients with pche levels between 10-20%. Though positive correlation exists among all four groups with atropine requirement, statistically it was significant o between the first two groups(p value- 0.01) but not between the last two groups(p value-0.767) The reason could be that in this study only 1 patient had pche levels <10%

Serum amylase levels	Mean dose of atro	Mean dose of atropine needed in mg	
	Mean	Standard deviation	
<88 u/l	86.81	45.184	
>88u/l	260.33	241.872	

Table no: 15 shows association between serum amylase levels and mean dose of atropine needed

't' test -4.518 P value-0.001 Highly significant. Mean value of atropine needed for patients with normal serum amylase levels was 86.81mg whereas it was 260.33mg for patients with elevated serum amylase levels. This association was statistically highly significant.

Discussion

In our study, majority of patients were in the age group of 21-30 years (55%) followed by 25% of the patients were in the age group of 31-40 years of age. Totally 91.7% of patients were within 40 years of age. This is in comparison to studies done by A Goel et al¹¹, Reihman et al¹², kavya S.T et al¹³, shah harsh D et al¹⁴. The reason for high mortality in the age group 21-30 years could because of that, this age group was vulnerable to various emotional conflicts that occur during this phase of life. This study revealed a male preponderance (53.3%), females accounting for 46.7% of cases. The male to female ratio in this study is 1.14:1. Male preponderance was also reported in studies conducted by Rajeev H et al¹⁵, A Goel et al¹¹, kavya S.T et al¹³.

Majority of cases in our study (96.7%) had consumed poison with a suicidal intent. As OP compounds are generally available ready hand as pesticides and open access to these compounds at pesticide shops may be the reason for OP compounds to be used as a common mode of suicidal attempt. This is in comparison to values reported by kozaic et $al^{16}(85\%)$, A Goel et al^{11} (96.1%), and Reihman et al^{12} .

In the present study, the commonest symptom was nausea (91.7%) followed by vomiting (75%) and sweating in 60%. of the patients. Convulsions were seen in 6.7% of patients. These observations were comparable to the pattern reported by shah harsh D et al^{15} , Reihman et al^{12} , and Goel et al^{11} .

All patients included in this study had a characteristic smell of organophosphorus compound. The common clinical signs were fasciculations (75%), miosis (63%), Tachypnea (60%), Bradycardia (26%) These results are comparable to the studies of A Goel et al¹¹, Reihman et al¹², Shah Harsh D et al¹⁵ and APN Kumar et al¹⁷.,.

Respiratory failure requiring ventilator support was observed in 26.6% of patients in our study. This is in comparison to values obtained by shah harsh D et al¹⁵ (30%), kozaci et al¹⁶ (20%), A Goel et al¹¹ (34.95%).

100% of patients with normal(sub clinical) grade of poisoning did not require ventilator Support and 100% of patients with Pche levels <20% required ventilator support. Our study showed a highly significant correlation between PChe levels and the need for ventilator support. Kavya S.T et al¹³ in their study found that 100% of the patients with pche levels <20% required ventilator support. Rajeev H et al¹⁵ found a direct correlation between the degree of inhibition of PChe levels and the severity of poisoning in their study, 11 out of 13 (84%) patients with pseudo cholinesterase levels less than 20% required ventilator support . Similar findings were observed in studies conducted by Reihman et al¹², Sumathi et al ¹⁸, weissmann-brenner et al ¹⁹, Goswamy et al^{20} , and Ahmed et al^{21} .

POP scale was calculated for all patients on admission. 70% of patients had mild grade of poisoning and 26.7% had moderate grade of poisoning. 2 patients (3.3%) in our study belonged to severe grade of poisoning. The individual components of POP scale namely miosis, fasciculation, respiratory rate, bradycardia and level of consciousness were compared with need for ventilator support. The findings in this were similar to the finding noted by , Reihman et al¹² and kavya S.T et al¹³.,

In this study serum amylase levels were found to be elevated in 18 (30%) out of 60 patients. Lee WC et al^{22} and Singh s et al^{23} reported hyperamylasemia to be present in 36% and 46.95% of the poisoned patients respectively.

Only 9.5% of the patients with normal serum amylase levels required ventilator support whereas 66.7% of the patients with elevated serum amylase levels required ventilator support. These results were statistically highly significant. (pvalue -0.001) N Matsumiya et al⁹ in their study found that, Of the 32 OP poisoning patients, 16 developed respiratory failure and received ventilator support. An increase in plasma amylase above the normal range was found in patients who developed respiratory failure and concluded that in OP poisoning, the elevation of amylase levels was predictive of subsequent respiratory failure. Studies done by sumathi et al¹⁸ and Kozacı et al¹⁶ also reported that the elevation of amylase levels was predictive of subsequent respiratory failure and requirement of mechanical ventilation

Mean dose of atropine required for patients with mild grade of POP scale was 86.76 mg and for patients with severe grade of pop scale was584 mg. These results are statistically significant(p value<0.005). A study conducted by shah harsh D et al¹⁵ showed that the total amount of atropine needed to treat the patients were increased with severity of POP scale which was statistically significant (P<0.05). Reihman et al¹² found that higher the pop scale grade higher the amount of atropine needed. Mean dose of atropine required for patients with normal pseudo cholinesterase levelsis72.69 mg whereas patients with pche levels <10% required 230 mg which is statistically significant. Reihman et al¹² in their study found that the serum cholinesterase at presentation appeared useful to assess severity of poisoning, particularly in terms of higher amount of atropine requirement.

Mean dose of atropine required for patients with normal amylase levels (<88U/L) was 86.81mg, whereas it was 260.33 mg for patients with elevated serum amylase levels .This association was statistically highly significant (p value-0.001). Kozaci et al¹⁶ in their study found that mean dose of atropine required for patients with serum amylase levels >300U/L was 532 mg and it was 295 mg for patients with serum amylase levels <300 U/L.

In this study, patients on ventilator required 290.38 mg (mean value) of atropine and patients not requiring ventilator required only 83.77 mg of atropine (mean value). P value is 0.001 which was highly significant. kozaci et al¹⁶., in their study found that high doses of atropine are required in patients with respiratory failure. The mean dose of atropine given to patients requiring ventilator support was 461 mg whereas it was 51 mg for patients without requiring ventilator support In a study done by Rajeev H et al¹⁵.,found that initial bolus atropine requirement to produce signs of atropinization strongly influenced ventilator assistance .Patients requiring more than 60 mg of atropine were more prone (all13patients-100%) for ventilator support as against none among patients with atropine requirement of less than 35 mg.

In our study Patients who survived required mean dose of 135.21 mg whereas patients who expired required 166.57 mg. The results in the present study are comparable with the studies by Reihman et al^{12} , S Singh et al^{23} .

Conclusions

 Pseudo cholinesterase levels were significantly depressed in patients who required ventilator support and correlated well with need for ventilator support as well as outcome.

References

- Miosis, bradycardia, increased respiratory rate, impaired level of consciousness and convulsions all associated well with need for ventilator support.
- Serum amylase levels correlated well with the severity of poisoning in terms of predicting the need for mechanical ventilation and dose of atropine required.
- the severity grade of poisoning As increased. atropine requirement also increased (.i.e., patients with elevated serum amylase levels, depressed pseudo cholinesterase levels and higher grade on POP score required higher doses of atropine when compared to patients with normal serum amylase levels, normal pseudo cholinesterase levels and lower grade on POP score.)
- There was a good association among the 3 parameters in the study (i.e., POP score, Pche levels, serum amylase levels) on admission.
- In case of high POP score, high and low levels of serum amylase and plasma cholinesterase respectively on admission, transferring the OP poisoning patient to a high dependency area like Respiratory Intensive Care Unit significantly improves the survival even in severe OP poisoning.
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