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### A Study of Possible Prognostic Predictors of Organophosphorus Poisoning

Ruksana Hamid, Suhail Sidiq, Abdul Qayoom lone, Mohammad Akbar Shah, Abdul Waheed Mir Department of Anaesthesiology and Critical Care SKIMS Soura

\*Corresponding Author:

Suhail Sidiq

Assistant professor Critical Care medicine SKIMS Soura

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#### ABSTRACT

Background: Organophosphorus poisoning can result from occupational, accidental or intentional exposure. It is of great concern in developing world as it affects the most productive age group of the society and has a high case fatality rate. Death is usually due to cardiovascular and respiratory failure. Early recognition of high risk cases is invaluable particularly in resource constrained settings, regarding referral to a higher center for intensive care.

Aim: To evaluate various parameters that can predict morbidity and mortality of acute organophosphorus poisoning.

Material and methods: A prospective hospital based study was conducted over a period of two years to evaluate the possible impact of age, Glasgow coma scale (GCS) on presentation, arterial oxygen saturation (SpO2%) on room air at presentation, time elapsed since exposure (in hours), blood pH, serum electrolyte levels and serum acetylcholinesterase levels on mortality and morbidity of patients of organophosphorus poisoning.

Results: The study revealed that the patients with GCS score <8, time since exposure >4.5 hours and serum acetylcholinesterase level <2300 IU/l at presentation have greater morbidity in our set up. Also the patients with GCS score <8, time since exposure >4.5 hours, serum acetylcholinesterase level <1800 IU/l, SpO2% <85% on room air,  $p^{H}$  < 7.25 and serum sodium level >150mmol/l on presentation have greater mortality.

Conclusion: It is suggested that the patients with these parameters should be immediately referred to an intensive care unit with possibility of need for mechanical ventilation.

Keywords: Organophosphorus compounds, morbidity, mortality, poisoning.

#### INTRODUCTION

Organophosphorous (OP) compounds are widely used as insecticides in the agricultural parts of the world.<sup>1</sup> Its poisoning, both intentional and accidental, is a major global problem with a case fatality rate of 4-30%. It is of great concern in developing world as it incidence is higher in young, economically active 2,3,4 society. Toxicity the group of of organophosphorus compounds is the result of inhibition of acetylcholinesterase. The rapid accumulation of acetylcholine in the synaptic junctions of CNS and peripheral tissues results in range of muscarinic, nicotinic and central effects.<sup>5</sup> Intermediate syndrome or type II paralysis usually occurs after 24-96 hours after acute cholinergic crisis.<sup>6</sup> Death usually occurs due to cardiovascular and respiratory failure.<sup>7</sup> The initial management of

acute OP poisoning includes cardiorespiratory stabilization, decontamination, gastric lavage and activated charcoal.<sup>8</sup> The mainstay of treatment is atropine and pralidoxime.<sup>9</sup>

A number of systems have been proposed for predicating outcome in OP poisoning, some rely on laboratory tests and others that use clinical parameters. The present study was conducted to evaluate possible predictors of mortality and morbidity of acute OP poisoning. Early recognition of these factors will help in appropriate allocation of resources, including intensive care unit in a resource constrained setting.

#### Material and methods

Our study was a hospital based prospective study conducted over a period of two years in a tertiary care facility. Following approval by institutional ethical committee and informed patient/attendant consent, all the patients of organophosphorus (OP) poisoning, diagnosed on the basis of clinical history and examination were included in the study. After initial assessment and resuscitation, all the patients were followed till the time of discharge/death and evaluated using following parameters

1. Age

2. Glasgow coma scale (GCS) on presentation

3. Arterial oxygen saturation (SpO2%) on room air at presentation.

- 4. Time elapsed since exposure (in hours)
- 5. Blood pH
- 6. Serum electrolyte levels
- 7. Serum acetylcholinesterase levels

The possible impact of these parameters on mortality and morbidity factors i.e, duration of hospital stay, need of admission to intensive care unit(ICU), and mechanical ventilation was also assessed.

### Statistical analysis

The data was analyzed using SPSS software version 20. The variables of interest were tabulated in terms of frequency and percentage. Pearson's chi square test was used to calculate p value. A two- tailed p- value less than 0.05 was considered to be statistically significant.

### Results

A total of 102 cases of OP poisoning were included in the study over a period of two years and evaluated for various parameters. Majority (54.9%) of the patients belonged to the age group of 15-25 years. Total number of male patients were 33 (32.35%) with mean age of 24.64 years compared to females who constituted a total of 69 cases (67.64%) with a mean age of 26.02years. 86 (84.3%) cases were from rural areas while as only 16(15.7%) were from the urban areas. 50.9% (52) of the patients were married. Housewives were the largest group (37.25%) followed by students and farmers. A total of 99 cases (97.05%) had ingested the poison and rest of the three had inhaled the poisonous fumes while spraying. 97 cases had taken it with suicidal intent. Hospital stay was less than 7 days in 71 cases (69.6%) and more than that in rest of the cases. All the parameters were compared between patients with hospital stay of <7days and >7days [table-1]. Statistically significant differences were observed in GCS and serum acetylcholinesterase levels between the two groups. Significant association was observed between hospital stay of >7days and GCS score <8 (RR :4.58; logged RR : 1.52) and serum acetylcholinesterase level <2300IU/l (RR : 5.20; logged RR : 1.61) at presentation. 64 patients (62.7%) needed admission in ICU, out of which 62 required mechanical ventilation. These parameters were also compared between patients with or without admission to ICU [table-2]. Significant difference was found between time elapsed since exposure, GCS and serum acetylcholinesterase levels. Also significant association was observed between need for admission to ICU and time elapsed after ingestion>4.5hours (RR: 4.2; logged RR: 1.43), GCS score <8 (RR : 5.48; logged RR : 1.74) and serum acetylcholinesterase level <2300IU/l (RR : 4.36; logged RR 1.47) at presentation.

Statistically significant difference was obtained in the mean time elapsed after exposure, GCS score and serum acetylcholineesterase levels between the groups which did and did not require ventilation [table-3]. Association was observed to be significant between requirement of mechanical ventilation and time elapsed after ingestion >4.5hrs (RR : 4.37 ; logged RR : 1.47), GCS score <8 ( RR : 4.48; logged RR : 1.49) and serum acetylcholinesterase level<2300IU/1 (RR :5.28; logged RR : 1.66).

Out of 62 cases, 8 were ventilated for more than 3 days. Statistically significant difference was noted only between serum acetylcholinesterase levels between the patients requiring ventilation <3 days and >3 days [table-4]. Association was significant between duration of mechanical ventilation >3 days and serum acetylcholinesterase level <2300 IU/l (RR: 4.21; logged RR: 1.44).

15 cases expired yielding a mortality of 14.7%., all of whom were admitted in ICU. 8 died of

multi system failure, 5 due to respiratory failure and 2 due to circulatory failure.

Statistically significant difference was noted between mean of time elapsed after exposure, GCS score, serum acetylcholineesterase level, arterial oxygen saturation (SpO2%) on room air at presentation, blood pH and serum sodium levels between patients who survived and expired. [table-5]. Significant association was observed between mortality and time elapsed after exposure > 4.5hours (RR: 12.42; logged RR : 2.52), oxygen saturation <85% (RR : 11.25; logged RR : 2.42), GCS score<8 (RR : 8.42; logged RR : 2.22), serum sodium levels >150 (RR : 3.28; p<sup>H</sup><7.25 1.18), logged RR: and serum acetylcholinesterase level <1800IU/l (RR :5.76: logged RR : 1.75).

### Discussion

Organophosphorus poisoning is one of the most common poisoning in developing world due to their easy availability and ignorance about their proper handling and toxicity. Despite high mortality and complications associated with it, no definite prognostic criteria have been set, which might help to assess patients at presentation.

Studies have advocated use of various scales and parameters to assess the severity of poisoning and prognosis. Peradenya organophosphorus poisoning (POP) scale, modified Driesbach criteria, Glasgow coma scale, APACHE II, SAPS, SOFA, serum cholinesterase levels, serum amylase, serum lipase, creatinine kinase and prolonged QT interval are a few among them.<sup>10</sup>

Our study involving patients of OP poisoning was also conducted with the basic aim of identification of possible predictors of morbidity and mortality of acute OP poisoning from clinical parameters at presentation. We assessed the impact of age, GCS at presentation, time elapsed since poisoning, SpO2 at presentation, blood pH, serum electrolytes and serum acetylcholinesterase levels at presentation on mortality and morbidity.

We found that mean GCS score at presentation was significantly higher in the patients who survived, those with shorter hospital stay, who were not admitted in ICU and did not require mechanical ventilation. The study also revealed a significant association between GCS score and mortality and morbidity factors. The findings are in accordance with studies conducted by Grmec et al,<sup>11</sup>Davies et al<sup>12</sup>, Deshpande et al,<sup>13</sup> and Mule<sup>14</sup> et al. GCS has the advantage of being practical in many clinical settings. It can be reliably used in identifying the patients who will potentially suffer respiratory failure. Its timely use can allow us to perform early triage at presentation itself. Similar results were obtained for acetylcholinesterase levels. Serum acetylcholinesterase levels at presentation were significantly higher in the patients who survived, those with shorter hospital stay, who were not admitted in ICU and did not require mechanical ventilation. This finding was consistent with studies conducted by Rehiman et al<sup>15</sup> Kang et al,<sup>16</sup>Many et al<sup>17</sup> and Banday et al.<sup>18</sup> Need of ventilation is also more in patients with low serum acetylcholinesterase levels. Thus serum acetylcholinesterase can be used for confirmation of diagnosis and for predicting patients who are at increased risk of mortality and morbidity.

Similarly more the time elapsed between consumption and initiation, more was the morbidity and mortality. This was similar to studies by Banday et al<sup>18</sup> and Ahmed et al<sup>19</sup>. Morbidity and mortality are directly proportionate to the lag time in initiation of treatment. The greater the delay in treatment, higher is the mortality and need for prolonged hospital stay, ICU admission and mechanical ventilation.

Oxygen saturation at room temperature at presentation was also higher in patients who survived than in those who expired. This was similar to the study conducted by Muley et al.<sup>14</sup>

Since severe OP poisoning can cause central respiratory depression, respiratory rate cannot be reliable guide to severity. Oxygen saturation at room air is a simple parameter to measure. It can be used in identifying the patients with high risk of death especially in a low resource setting.

The pH value of the patients that had died was significantly lower than those survived. This was consistent with findings of Liu et  $al^{20}$  and Gundaz<sup>21</sup> et al. The acid-base interpretation can be effective in quick diagnosis and prediction of the outcome of patients with acute OP poisoning. The presence of acidosis can be taken as independent predictor of mortality.

Our study also found significant association between mortality and serum sodium level of greater than

150mmol/l. Out of the 64 patients admitted in ICU 15 had hypernatremia. Among these 15 patients, 4 recovered and 11 expired. Linder et al and Waite et al also found hypernatremia to be common in ICU in general with incidence of 9% and 15% respectively. Development of hypernatremia was associated with increased mortality and length of stay inICU.<sup>22,23</sup> Although the cause of hypernatremia could not be elucidated, it may be due to alteration in membrane permeability due to alteration in membrane permeability due to excessive acetycholine level at the synapses.<sup>24</sup> The increased serum sodium level in our patients may also be due to the use of hypertonic saline for gastric lavage at peripheral hospitals. No study yet has established cause of hypernatremia in these patients. Hence further studies need to be done to determine the mechanism of hypernatremia in patients of organophosphorus poisoning in our setup.

#### Conclusion

We concluded that patients with GCS<8, arterial oxygen saturation on room temperature <85%, time since exposure >4.5hrs, serum Na>150, pH<7.25 and serum acetylcholinesterase levels <2300IU/l on presentation have greater morbidity and mortality in our setup. It is suggested that the patients with these parameters should be immediately referred to an ICU with possibility of need for mechanical ventilation. In resource constrained settings, identifying these parameters will help in decision making regarding referral to a higher center or keeping under observation, after initiation of treatment.

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#### Initial parameter Hospital stay<7days Hospital p Value stay>7days 0.777 Age in years 25.03 25.52 Time elapsed after ingestion( 4.52 5.00 0.494 in hours) Glasgow coma Scale(GCS) 10.38 7.35 0.0001 score Oxygen Saturation $SpO_2$ (%) on 89.76 83.10 0.234 room air 7722.37 9135.35 Total leukocyte count(TLC) 0.106 139.97 Serum Sodium (mmol/l) 142.74 0.484 Serum Potassium (mmol/l) 3.14 2.98 0.350 7.28 Ph 7.30 0.408 Serum acetylcholine esterase (IU/L) 2264.2 3510.4 0.0001

#### Table 1: Comparison of the Initial Parameters between Patients with Hospital Stay Days

## Table-2 Comparison of the Initial Parameters in Patients with or Without Admission to Intensive Care Unit (ICU)

Initial parameter	Not Admitted to ICU	Admitted to ICU	p Value
Age in years	23.42	26.22	0.086
Time elapsed after exposure ( in hours)	2.07	4.67	≤0.0001
Glasgow Coma Scale (GCS) score	14.05	6.73	≤0.0001
Oxygen Saturation SpO <sub>2</sub> (%) on room air	88.16	82.10	0.232
Total leukocyte count (TLC)	8152.99	8136.3	0.986
Serum Sodium (mmol/l)	139.61	144.63	0.225
Serum Potassium (mmol/l)	3.14	3.01	0.348
рН	7.25	7.23	0.627
Serum acetylcholine esterase (IU/L)	4792.45	2145.63	≤0.0001

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# Table 3: Comparison of the Initial parameters in Patients With or Without Requirementof Mechanical Ventilation

Initial parameter	Not ventilated	Required ventilation	p Value
Age in years	23.42	26.32	0.084
Time elapsed after exposure( in hours)	2.07	4.59	≤0.0001
Glasgow Coma Scale(GCS) score	14.15	6.78	≤0.0001
Oxygen saturation SpO <sub>2</sub> (%) on room air	88.66	83.16	0.334
Total leukocyte count(TLC)	8154.99	8234.33	0.968
Serum Sodium (mmol/l)	138.91	142.63	0.215
Serum Potassium (mmol/l)	3.24	3.11	0.368
рН	7.31	7.26	0.518
Serum acetylcholine esterase (IU/L)	4762.45	2125.63	≤0.0001

## Table 4: Comparison of the Initial Parameters between Patients with Duration of Mechanical<br/>Ventilation <3 days and > 3 days

Initial parameter	Duration <3 days	Duration >3 days	p Value
Age in years	25.77	29.38	0.234
Time elapsed after exposure( in hours)	4.62	5.00	0.493
Glasgow Coma Scale(GCS) score	6.80	6.25	0.289
Oxygen Saturation SpO <sub>2</sub> on room air (%)	87.66	84.10	0.354
Total leukocyte count(TLC)	9140.11	6875.00	0.202
Serum Sodium (mmol/l)	138.61	143.63	0.250
Serum Potassium (mmol/l)	3.61	3.07	0.111
рН	7.26	7.24	0.657
Serum acetylcholine esterase (IU/L)	3512.44	2268.26	≤0.0001

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Initial parameter	Survived	Expired	p Value
Age in years	24.76	27.60	0.851
Time elapsed after exposure( in hours)	3.46	5.10	≤0.0001
Glasgow coma Scale(GCS) score	10.16	5.40	≤0.0001
Oxygen saturation SpO <sub>2</sub> (%) on room air	89.72	73.87	≤0.0001
Total leukocyte count(TLC)	8154.99	8133.33	0.985
Serum Sodium (mmol/l)	140.90	154.87	≤0.0001
Serum Potassium (mmol/l)	3.12	3.08	0.2166
рН	7.35	7.22	≤0.0001
Serum acetylcholine esterase at presentation (IU/L)	3367.57	1763.60	≤0.0001

#### Table 5: Comparison of the Initial Parameters between Patients who Survived and Expired

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