Original Article

Cholinesterase Level in Erythrocyte or Serum: Which is More Predictive of the Clinical Outcome in Patients with Acute Organophosphate Poisoning?

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Received: 28.06.2018 *Accepted: 13.08.2018*

ABSTRACT

Background: Acute organophosphate poisoning (AOPP) is related to several clinical complications that may be fatal. The aim of this study was to evaluate the effects of demographic, clinical and laboratory findings on AOPP outcome.

Methods: In this retrospective cross-sectional study, medical records of all patients with AOPP admitted to Imam Reza Hospital, Mashhad, Iran, were reviewed from January 2016 to December 2017. Demographic data, clinical presentations, erythrocyte cholinesterase (RBC-ChE) and serum cholinesterase (S-ChE) activities were studied and evaluated in relation to clinical outcome of the patients.

Results: A total of 64 patients (37 male, 27 female) were evaluated from whom 6 patients (9.4%) died. Statistically significant relationships were found between the outcome of the patients and RBC-ChE activity (p =0.008), intratracheal intubation (p=0.003), and abnormal blood pressure (p =0.009). Despite the lower mean S-ChE levels in the deceased patients and loss of consciousness in 42.2% (n=27) of patients, there was no statistically significant correlations between these factors and patients' outcome (p =0.147, p =0.075, respectively).

Conclusion: RBC-ChE activity, need for intratracheal intubation, and abnormal blood pressure on admission were important predictive factors in the clinical outcome of AOPP. Although S-ChE activity, level of consciousness, white blood cell count and blood glucose level on admission provide useful information, these data had no prognostic value in patients with AOPP.

Keywords: Acetyl Cholinesterase, Organophosphate Poisoning, Patient Outcome Assessment, Serum Cholinesterase.

IJT 2018 (5): 23-26

INTRODUCTION

Acute organophosphate poisoning (AOPP) is a major health problem in the developing countries and is also responsible for many deaths in the world annually [1-4]. Because of the high mortality and morbidity of AOPP, rapid diagnosis and treatment are often necessary [5-7]. The causes of acute cholinergic syndrome include increased accumulation of acetylcholine, decreased degradation of acetylcholine and overstimulation of the central and peripheral muscarinic and nicotinic receptors [1-3]. Although, erythrocyte acetylcholinesterase (RBC-AChE) inhibition, unlike decreasing activity of serum cholinesterase (S-ChE) or plasma butyrylcholinesterase (BChE), had more correlation with cholinesterase level in the synapses and neuromuscular junctions and consequently with clinical manifestations, however, both RBC-AChE and S-ChE should be assessed in AOPP [6-8]. Common clinical manifestations of AOPP include bradycardia, miosis, bronchospasm, bronchorrhea, salivation, lacrimation, diarrhea, urination, muscle weakness, and fasciculation [9-11]. Moreover, important clinical presentations include central nervous system (CNS) depression, convulsions, respiratory failure, hypotension with impaired neurological function and cognition, causing severe disability in the victims [9, 12, 13].

In the related literature, different predictors have been suggested for determining severity or prognosis of AOPP including patient age [14]; some clinical presentations such as miosis [15], bradycardia[14]; fasciculations [15], low Glasgow Coma Scale (GCS) score [1, 15-17], APACHE II score [18], QTC interval prolongation [19]; laboratory findings including blood glucose level [14], leukocytosis [20], acidosis [14], serum bicarbonate [18], serum lactate [21], high creatinine [16], serum amylase [22]; serum lipase [22], lactate dehydrogenase [14]; creatine phosphokinase [22]; decreased RBC-ChE activity [2, 17, 23]; and low S-ChE activity [2, 16, 17, 24]. Due to inconclusiveness in prognostic factors, the aim of this study was to assess the relationship among the demographic, clinical, and laboratory findings, and the clinical outcome of the patients with AOPP.

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MATERIALS AND METHODS

In this retrospective cross-sectional study, all patients with AOPP who had been admitted to the poisoning emergency department (ED) of Imam Reza Teaching Hospital, Mashhad, Iran, were evaluated for inclusion in the study between January 2016 and December 2017. In each case, the diagnosis had been made based on history gathered from the patient or his/her relatives. The hospital's clinical toxicologists also had visited the patients and provided further information to establish the diagnosis on admission to the ED. These patients were subsequently managed in the hospital intensive care unit (ICU) or the poisoning ward. Relevant data were also extracted from the patient's medical records, if available. No personal identification data were recorded and all information was kept strictly confidential. Approval for performing the study was issued by the Ethics Committee, Research and Technology Deputy, Mashhad University of Medical Sciences, Mashhad, Iran.

To conduct this study, we included all patients with AOPP at ages of 14 years or older who admitted to the hospital during the study period. Patients who did not have complete laboratory tests or had co-ingestion of other xenobiotics were excluded from the study. The collected information for each case were: 1) Age, 2) Gender, 3) Marital status, 4) Date of admission, 5) Length of hospital stay, 6) Initial laboratory findings (RBC-ChE, S-ChE, leukocytes count, blood glucose level), 7) Blood pressure on admission, 8) GCS score, 9) Intratracheal intubation, and 10) the patients' clinical outcome. In-hospital fatality considered as the primary outcome. The data were analyzed using SPSS version 19, with the descriptive statistical data presented as the mean ± standard deviation (SD) and percentage as appropriate. The data consisted of the demographic characteristics and clinical outcomes for every patient. The variables were also grouped into survivors and non-survivors. Student *t*-test was used to examine the differences in the quantitative variables with normal distributions. Mann–Whitney *U*-test was used to examine the differences in quantitative variables with abnormal distributions. The relationship between categorical variables and the outcome were also evaluated, using Fisher's exact test for all cases. A confidence interval of 95% and a *p*-value of <0.05 were considered as being statistically significant.

RESULTS

Of the 64 studied patients, the majority were male (57.8%) with the youngest being 13 and the oldest being 82 years old. The mean ± SD of patients' age and length of hospital stay were 31.34 ±15.42 years and 5.5± 6.12 days, respectively. The in-hospital fatality rate was 9.4% (n=6) including five men (83.3%) and one woman (16.7%). Remainder of patients (n=58, 90.6%) had been recovered and discharged from the hospital without any prominent complications. The lowest RBC-ChE and S-ChE levels were 0.6 and 204 IU/L, respectively. Among the deceased patients, the highest RBC-ChE and S-ChE levels were 2.7 and 1270 IU/L, respectively. Table 1 represents the demographic and some clinical characteristics of the studied patients.

All patients had ingested organophosphorus compounds orally for deliberate self-harm or to commit suicide and other routes of intoxication were not observed among the studied patients. The clinical characteristics and outcome of the patients are presented in Table 2. Leukopenia and leukocytosis were seen in 1.5% (n=1) and 48.4% (n=31) of patients, respectively. Hypotension and hypertension were observed in 3.1% (n=2) and 15.6% (n=10) of the patients, respectively. Hypoglycemia and hyperglycemia were found in 9.3% (n=6) and 37.5% (n=24) of the patients, respectively.

As shown in table 2, there were statistically significant correlations between RBC-ChE activity (P=0.008) and abnormal blood pressure (P=0.009) with the in-hospital fatality. There were no statistically significant relationships between abnormal white blood cells (WBC) count or abnormal blood glucose levels on admission and death.

Table 1. Demographic characteristics of patients with organophosphate poisoning.

Patients Characteristics	Number & Percentage
Gender	
Male	37 (57.8%)
Female	27 (42.2%)
Age (years)	
Mean ± SD	31.3 ± 15.4
Range	13 - 82
Marital Status	
Married	37 (57.8%)
Single	23(35.9%)
widow	4 (6.3%)
Duration of hospital stay (days)	
Mean ± SD	5.5 ± 6.12
Range	1 – 30
Patient Condition	
Recovered & discharged	58 (90.6%)
Died	6 (9.4%)

Table 2. Effect of some studied factors on clinical outcome of the patients with acute organophosphate poisoning.

Factor	Number of patients			P-value
	Total	Recovered	Died	
S-ChE (IU/L) Median (min-max)	902 (125-8054)	960 (12-8054)	573 (204-1270)	0.147 (Mann-Whitney U)
BG (mg/dL) Median (Min-Max)	109 (22-364)	111 (59-364)	66 (22-233)	0.157 (Mann-Whitney U)
RBC-ChE (IU/L) Mean ± SD	2.59 ± 1.71	2.72 ± 1.72	1.30 ± 0.88	0.008 (*t*-test)
WBC count/mm^3 Mean ± SD	12.6 ± 5.51	12.36 ± 4.65	15.76 ± 11.12	0.49 (*t*-test)
Loss of Consciousness (n)	27 (42.2%)	22 (81.5%)	5 (18.5%)	0.075 (Fisher's Exact Test)
Intratracheal Intubation (n)	16 (25%)	11 (68.7%)	5 (31.3%)	0.003 (Fisher's Exact Test)
Abnormal BP (n)	12 (18.8%)	8 (66.7%)	4 (33.3%)	0.009 (Fisher's Exact Test)

S-ChE: serum cholinesterase level; RBC-ChE: Red Blood Cells acetylcholinesterase level; BG: Blood Glucose; WBC: White Blood Cells; BP: Blood Pressure

DISCUSSION

Organophosphorus pesticide self-poisoning is an important clinical problem in developing and middle-income countries and kills an estimated 200,000 people every year [7]. Unfortunately, most patients are young and in productive ages. In our study, the mean age of the patients was 31.3 (range, 13-82) years which was consistent with other studies in which mean age of patients were reported as 32.4 years (range, 13-94) [16]; 37 (range, 20-80) years [1] and 56 (range, 16-88) years [18], respectively.

We found significant correlations between RBC-ChE, intratracheal intubation, and abnormal BP and clinical outcome of the patients, but there were no correlations between outcome and other factors such as initial GCS score, S-ChE level, and leukocytosis. Similar to our study, some authors suggested that serum cholinesterase level is not useful in predicting the clinical prognosis and it must be interpreted carefully [1, 4, 24, 25]. Moon et al. suggested that decrease in both RBC-ChE and S-ChE levels and the associated clinical findings should be considered together for a comprehensive patient evaluation and clinical management. They also concluded that RBC-ChE activity is a useful variable in predicting the minimum length of time that the patient needs to be on mechanical ventilation [26]. Cander et al. (2011) reported no established prognostic value for S-ChE or leukocytosis, but GCS values have been found to be effective in predicting the outcome [1]. Another study also reported a predictive value for GCS in organophosphate poisoning and suggested that patients with a GCS value under 13 must be closely managed even if they do not have poisoning symptoms on admission [27].

In previous studies, the reported rates of leukocytosis were between 30% and 76% [1, 20, 28] whereas the leukocytosis rate was found to be 48.4% in our study. However, a statistically significant correlation was not found between the leukocyte count and the duration of hospital stay or mortality, although there was a considerable leukocytosis in deceased patients. Similarly, there was no statistically significant correlation between the leukocyte levels and the clinical outcome in the reviewed literature [1, 20, 28]. Conversely, Kumar et al. (2018) in a prospective, observational clinical study on 80 patients suspected of AOPP at a tertiary rural teaching health-care in India concluded that leukocyte count on admission can be used as a prognostic marker with OP poisoning [29].

However, it seems that the observed inconclusiveness in the literature regarding predictive or prognostic factors in AOPP may be related to different clinical settings, patient characteristics, type and toxicity of ingested organophosphate pesticides, and management modalities.

However, medical management of AOPP is difficult, with case fatality generally more than 15% [7]. In our study, the in-hospital fatality was 9.4%. One study concluded that rapid diagnosis and utilization of proper treatment regimen can reduce the mortality to less than 15% [28]. The lower mortality in this study in comparison to other studies may be associated to immediate evaluation and management of our patients in hospital or perhaps is related to low toxic nature of currently used organophosphorus pesticides in Iran. The main limitation of this study was the shortage of information about the type of organophosphate compounds that had been ingested by the patients.

CONCLUSION

Establishing the relevant prognostic factors in the clinical setting is crucial for the management of patients with acute organophosphate poisoning. This study demonstrated that RBC-ChE level, abnormal blood pressure on admission and the initial need for intra-tracheal intubation significantly correlated with the patients' in-hospital fatality and may be considered as important prognostic factors in evaluation and treatment of acute organophosphorus pesticides poisoning. Conversely, abnormal levels of S-ChE, blood glucose level and leukocytosis did not provide significant prognostic values for predicting the in-hospital outcomes of the patients. Further studies will be required to elucidate definitive prognostic factors in patients suffering from acute organophosphate poisoning.

ACKNOWLEDGEMENTS

The authors would like to acknowledge Mrs. Hoseini, Director of the Medical Record Department, Imam Reza Hospital, Mashhad, Iran, for providing the required patients' data for conducting this study.

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