REVIEW

Does organophosphate poisoning cause cardiac injury?

Abbas Aghabiklooei[1*], Babak Mostafazadeh[2], Esmaeil Farzaneh[3] and Afsaneh Morteza[4,5]

[1]Department of Forensic Medicine and Toxicology, Tehran University of Medical Sciences, Tehran, Iran
[2]Department of Forensic Medicine and Toxicology, Shahid Beheshti University of Medical Sciences, Tehran, Iran
[3]Department of Forensic Medicine and Toxicology, Ardabil University of Medical Sciences, Ardabil, Iran
[4]Tehran University of Medical Sciences, Tehran, Iran

Abstract: Organophosphates are insecticides which are widely used as a suicidal agent in Iran. They are associated with different types of cardiac complications including cardiac arrest and arrhythmia, however their role in cardiac injury is not known yet. The aim of this study was to investigate the presence of myocardial damage in patients with cholinesterase poisoning.It was a prospective study conducted from January 2008 to March 2010. Cohorts of patients with cholinesterase poisoning due to suicidal attempt who have been referred to Loghman hospital were selected. Patients who have taken more than one poison or were used concomitant drugs were excluded. Physical examination was performed on admission to discover warning sign. Peripheral arterial blood gases, creatine kinase, creatine kinase-myocardial band, troponin-T measurements were performed in all cases. There were 24 patients, 7 of them women, with the mean age of 41.2±15.05 who were included in this study. Non-survivors had significantly higher levels of systolic blood pressure, partial pressure of oxygen in arterial blood, partial pressure of carbon dioxide, bicarbonate Glasgow Coma Scale scoring and longer duration of mechanical ventilation. Our findings showed that cardiac injury is an important cause of death in organophosphate poisoning. It could be hypothesized that cardiac injury is a strong predictor of death in patients with organophosphate poisoning.

Keywords: Organophosphates, poisoning, heart.

INTRODUCTION

Organophosphates are insecticides used against insects in all developed forms, but mainly to kill mature insects (Diaz, 2008). They are irreversible cholinesterase inhibitors with potential human toxicity (Kucukkilinc *et al*., 2010). They have a great danger as each year nearly 21% of poisoned patients die due to suicidal attempts in Iran (Noshad *et al*., 2007, Abdollahi *et al*., 1997).

Respiratory paralysis and cardiac arrest are considered as the most common causes of death in these patients (Noshad *et al*., 2007, Goel and Aggarwal, 2007). They are associated with sensory-neural hearing loss in workers exposed to pesticides (Hoshino *et al*., 2008). it is also associated with altered neuromuscular function (Jayawardane *et al*., 2009). There is a wide variety in clinical features and timing of onset (Akyildiz *et al*., 2009, Singh and Khurana, 2009). Depending on the particular type of organophosphate involved. Recent studies have emphasized cardiac arrest (Fukushima *et al*., 2010) and complete heart block (Siegal *et al*., 2009) as the causes of death in acute organophosphate poisoning. To date we are unaware of any study demonstrating cardiac injury by organophosphate poisoning. The aim of this

study was investigate whether or not myocardial damage occurs in patients in cholinesterase poisoning.

METHODS

It was a prospective study conducted from January 2008 to March 2010. Cohorts of patients with cholinesterase poisoning due to suicidal attempt who have been referred to teaching loghman hospital were selected. A detailed medical and family history including route of entrance of the poison and the time interval between exposure and hospital arrival was obtained from all subjects. Patients who have taken more than one poison or were used conc-omitant drugs were excluded. Physical examination was performed on admission to discover warning signs includ sweating, increased levels of body secretions, pulmonary edema, myoclonus, urinary incontinence, cyanosis, and the presence of seizure on or before admission. Glasgow Coma Scale (GCS) scoring was measured for all patients. The occurrence of newly diagnosed signs and symptoms was also included. ECG monitoring was performed for all patients'. The examination took place during patient's resuscitation and atropine treatment.

All patients received standard medical treatment under the supervision of consultant physicians. This followed a

Corresponding author: e-mail: mstzbmd@sbmu.ac.ir

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standard protocol according to patient's clinical condition. The protocol included basic life support treatments include suction of oral secretions, intubation, and positive pressure mechanical ventilation. Intravenous fluids are usually given as soon as there is venous access and blood is drawn for laboratory investigation. Rapid atropinesation, with doubling doses of atropine at 5 to 10 minutes intervals, starting at 1-3mg, given until improvement of muscarinic signs, was performed for all patients. All symptomatic patients received pralidoxime chloride 1g IV four times a day for one to three days. Peripheral arterial blood gases, creatine kinase (CK), creatine kinasemyocar-dial band (CK-MB), and troponin-T measurements were performed in all cases

STATISTICAL ANALYSIS

The statistical package SPSS 16 for windows (Chicago, Illinois, USA), was used for analysis. Kolmogorov-Smirnov test was employed to test the normality of the variables. Variables distributed normally are presented as mean ± standard error of mean (SEM). Variables with skewed distribution are presented as median [interquintile range]. To further study the factors associated with death in our studies population, we stratified the patients into survived and non-survived groups accordingly. Student t test or Mann Whitney U test was employed to compare continuous variables between groups as appropriate, Categorical variables are analyzed using chi square test. Logistic regression modeling was employed to predict the outcome of the patients according to their symptoms on admission and serum markers of cardiac injury.

RESULTS

There were 24 patients, (Seven female and Seventeen male and F/M ratio of 1/2.4), with the mean age of 41.2± 15.05 who were included in this study. Characteristics of

participants and their symptoms on admission are presented in table 1. Patients in survived and non-survived group did not differ in initial symptoms on admission, amount of ingested poison, duration of stay in hospital, respiratory rate, pulse rate, temperature and cholinesterase levels. Non-survivors had significantly higher levels of systolic blood pressure, partial pressure of oxygen in arterial blood, partial pressure of carbon dioxide, bicarbonate, Glasgow Coma Scale scoring and longer duration of mechanical ventilation (table 2). Serum Markers of cardiac injury was significantly higher in non-survivors in comparison with survived patients (fig. 1).

DISCUSSION

Organophosphate poisoning had a higher level of markers of CK-MB, Troponin and CK-Total. We also demonstrated our data demonstrated that survived patients from that patients who died did not differ in duration of admission in hospital and estimated amount of ingested poison in comparison with survivors. To date, we are unaware of any study demonstrating higher serum levels of cardiac markers as a predictor of death in patients with organophosphate poisoning. Although these findings do not allow us to determine whether cardiac injury was the leading cause of death in these patients, it supports the hypothesis that cardiac injury is a strong predictor of death in patients with organophosphate poisoning.

There is a very few studies investigating the correlation between cardiac injury and intoxication. In a prospective study investigating the role of acute CO poisoning on cardiac injury suggested that it is not necessary to routinely measure CK, CK-MB and troponin-T in intoxicated patients (Aslan *et al*., 2005). In the other hand some studies have suggested CO poisoning as a finding of myocardial damage in patients with CO poisoning seems to indicate an unfavorable long-term prognosis, although

Table 1: Characteristics of patients with acute organophosphate poisoning

Characteristics	Value n=24
Age , years	41.21±15.05
Women (n, %)	7(29.2%)
Estimated amount ingested, ml	371.46±174.2
Time interval between exposure and hospital arrival, Hours	7.46±5.10
Death (n, %)	9 (37%)
Ventilation required (n, %)	10 (42%)
Symptoms on admission (n, %)	
Sweating, n (%)	22 (91%)
Increased amount of body secretions, n (%)	16 (67%)
Pulmonary edema, n (%)	17 (71%)
Meiotic pupils, n (%)	14 (58%)
Myoclonus, n (%)	2 (8%)
Urinary incontinence, n (%)	8 (33%)
Cyanosis, n (%)	1 (4%)
Reduced GCS, n (%)	1 (4%)

Table 2: Comparison of serum markers of cardiac injury, initial and later parameters between survivors and non survivors

	Death n=9	Survival n=15	P value
Estimated amount ingested (ml)	303.2±152.9	412.2±178.3	NS
Glasgow Coma Scale on admission	10.6±2.74	14.1±0.756	0.001
Cholin Esterase levels (U/L)	303±50.9	412±45.9	0.17
CK_total (ng/mL)	246.9±114.9	133.20±84.1	0.025
Tpn_I (ng/mL)	8.57±4.9	3.98±11.65	0.001
CK_MB (ng/mL)	148.64±103.9	17.7±29.1	0.001
Duration of stay in Intensive Care Unit, (days)	4.5±2.6	2.27±1.5	0.025
PCO2, (mmHg)	59.6±7.1	50.8±4.475	0.003
Duration Of stay in Hospital, (days)	4.6±2.4	4.27±1.8	NS
PaO2, (mmHg)	72.7±8.8	89.4±4.5	0.001
Mean duration of mechanical ventilation, (hrs)	3.7±1.56	1.07±0.26	0.001
Blood Pressure, (mmHg)	88.7±10.47	99.5±7.7	0.03
Respiratory Rate, (n/ minutes)	30.5±8.8	31.5±4.9	NS
Pulse Rate, (n/ minutes)	45.8±7.6	51.73±8.3	NS
Temperature	36.9±0.40	36.8±0.17	NS
PH	7.17±0.10	7.28±0.04	0.003
HCO3, (mmol/L)	17.1±2.26	20.6±1.8	0.001

Variables distributed normally are expressed as Mean ± Standard Error of Mean (SEM), CK: Creatine kinase, CK-MB: Creatine kinase-myocardial band, Tpn_I: Troponin, PaO2: Partial pressure of oxygen in arterial blood, PCO2: Partial pressure of carbon dioxide: HCO3: Bicarbonate
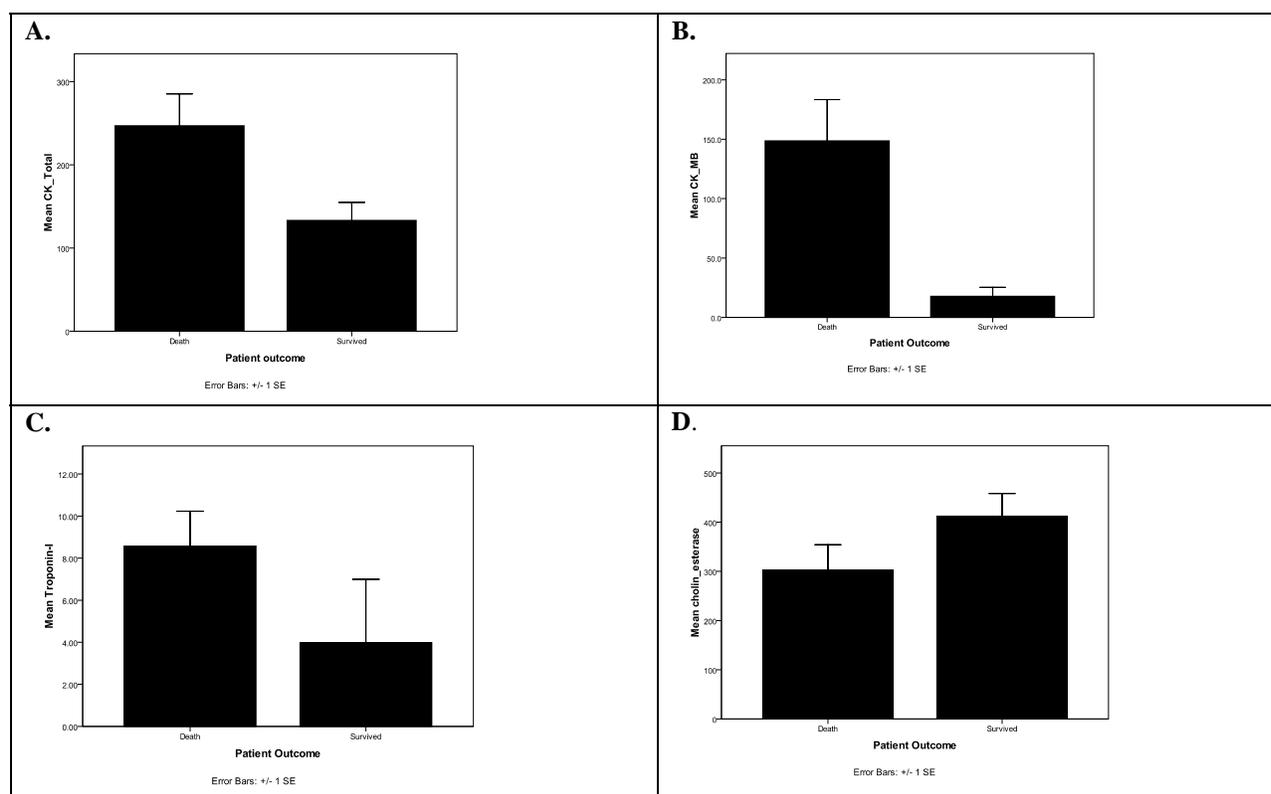
Fig. 1: Demonstrating the man of A: Total creatine kinase (CK-total), B: Creatine kinase-myocardial band (CK-MB), C: Troponin-I and D: Cholin Esterase in dead and survivors from organophosphate poisoning.
Bars represent the mean and the handles represent the standard error of mean

it needs further confirmation (Rastelli *et al*., 2009). Mortality from myocardial infarction was higher than expected in a five year cohort of patients working in iron mines of Netherlands (Bjor *et al*., 2009). Giermaziak H. (1989) suggested that, ECG records did not demonstrate myocardial necrosis in pesticide-poisoned patients

(Giermaziak, 1989). In consistent with our findings, in the

study conducted by Yavuz and collaborators cardiac poisoning due to organophosphate poisoning was associated with increased levels of serum Troponin-T level (Yavuz *et al*., 2008). Besides it is a predictor of mortality in organophosphate poisoned patients (Davies *et al*., 2008, Kao *et al*., 2009). We also did not found significant difference in cholinesterase levels between dead and survived patients. In consistent with our findings, it has previously shown that cholinesterase levels does not have a significant value in acute organophosphate poisoning (Nouira *et al*., 1994).

The principal limitation of the current study is its small sample size moreover we could not collect the name of the individual organophosphates that the patients used for suicide. In an interesting study by PayanRente and collaborators (2012), it was shown that organophosphate poisoning cause an increase in lipid per oxidation products. We did not found any other study show the effect of organophosphates on lipid levels; how ever this could be an interesting topic for future prospective studies. In conclusion we have shown increased serum markers of cardiac injury in patients died from organophosphate poisoning. This may add to the understanding of the organophosphate mechanisms of death in human.

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