Risk Factors for Mortality in Organophosphate Poisoned Patients

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ARTICLEINFO

Article Type:
Original Article

Article History:
Received: 9 Sep 2014
Revised: 20 Sep 2014
Accepted: 22 Oct 2014

Keywords:
Organophosphate
PR prolongation
Mortality

ABSTRACT

Background: Organophosphates (OP) compounds are used as insecticides in agricultural and domestic settings throughout the world. Acute pesticide poisoning has a high morbidity and mortality, especially in developing countries. The purpose of this study was to evaluate the data on acute adult organophosphate poisoning (OPP).

Methods: In Descriptive cross sectional study at Loghman Hakim Hospital in Tehran-Iran during March 2010 to June 2013 and identify the risk factors of mortality, patients with the primary diagnosis of OPP who were admitted to Loghman-Hakim Hospital Poison Centre (LHHPC) were the subjects of this prospective study. Cholinesterase (CE) activity and the PR interval was determined for each patient using the Bazett formula and considering >200 msec. as prolonged. Comparative outcomes of the study were respiratory failure, systolic blood pressure, GCS and intentional poisoning, analysis of the PR interval in the primary ECG on admission, and rate of mortality.

Results: The study included 201 patients with a diagnosis of OPP. The mean age of the patients was 33.93. The mortality rate was 9%. Nine patients had conductive abnormality (PR prolongation) in ECG. There was no significant difference between two groups (prolonged and normal PR intervals) according to respiratory failure and systolic blood pressure<90mm Hg and GCS and intentional poisoning. The mortality rate in the long PR group was significantly higher than that of the normal PR group.

Conclusion: In our study it has been well demonstrated that PR-interval prolongation affects mortality rate. Prolongation of the PR interval is associated with increased risks of mortality in OPP.

►*Implication for health policy/practice/research/medical education:* Risk Factors for Mortality in Organophosphate Poisoned Patients

► *Please cite this paper as:* Raouf-Yazdinejad S, Emamhadi MA, Okazi A, Memarian A. *Risk Factors for Mortality in Organophosphate Poisoned Patients*. *International Journal of Medical Toxicology and Forensic Medicine*. 2015; 5(2): 73-7.

1. Introduction:

Organophosphates (OP) compounds are used as insecticides in agricultural and domestic settings throughout the world (1). Acute pesticide poisoning has a high morbidity and mortality, especially in developing countries. The mortality rate of organophosphate poisoning varies from 10% to 86% (2). Accidental poisoning can occur after exposure through skin or inhalation and it can cause serious poisoning often following suicidal ingestion (3).

In Iran, organophosphate poisoning (OPP) is a major health problem, and OPs are the main cause of pesticide poisoning and pesticide-related deaths in Tehran (4). The cardiac complications associated with organophosphate poisoning are not fully appreciated by medical practitioners (5). So this study aimed to evaluate risk factors for mortality in organophosphate poisoned patients.

2. Materials and Methods:

In this Descriptive cross sectional study, 1047 patients with history of acute insecticide poisoning who admitted to the emergency ward of Loghman Hakim Hospital during March 2010 to June 2013, as a tertiary referral center in Tehran, Iran. During of our study, 1047 patients with history of acute insecticide poisoning admitted to the emergency ward of Loghman Hakim Hospital. Cholinesterase (CE) activity and the PR interval were determined for each patient using the Bazett formula and considering >200 msec as prolonged (6). Comparative outcomes of the study were respiratory failure, systolic blood pressure, GCS and intentional poisoning, PR interval in the primary ECG on admission, and rate of mortality. Qualitative data were expressed by mean±standard deviation (S.D) and frequency. For comparisons and determination of mortality and morbidity prognostic factors descriptive cross tab, Chi square and logistic regression test were applied by using SPSS software version 21. To control possible confounding factors, multivariate regression analysis was performed and significance level was considered at $P \leq 0.05$. It should be noted that this study approbated with the guidelines of the Declaration of Helsinki and approved by the Medical Ethics Committee of Loghman Hakim Hospital.

3. Results:

From 1047 patients, 201 patients included to our study with a diagnosis of OPP, that 18 OP poisoned died and 183 patients survived. Just 191 patients were evaluated for PR interval, because 10 patients did not have the first ECG at the time of admission. 16 dead patient with PR prolongation and 175 without PR prolongation were evaluated (Table 1). Overall, 95 (47.3%) were female and 106 (52.7%) were male. The mean age of the patients was 33.93 (SD=17.08), ranged from 2.5 to 89 years old. Various types of organophosphates was Diazinon, Malathion, Chlorpyrifos, Cyhalotrine, Zolone, Gusathion, Oxydemetonmethy, Pyrymphous methyl, Ethion, Bichon and Guthion(azinphos_methyl). Details have been shown in (table 2).

Methods of poisoning in 93.4% were oral and in 6.6% were other methods including inhalation, injection, conjunctiva and mixed. Use of OP was intentional in 85.8% of patients while 14.2% accidentally were poisoned.

PR prolongation more than 2 second was seen in 9 (4.7%) patients, while PR was less than 2 seconds in 182 (95.3%) patients.

Atropine was used in 180 (89.6%) and pralidoxim was used in 161 (80.1%) patients. Bradycardia was seen in 6 (3%) and tachycardia was seen in 50 (24.9%) patients. Mean of CE level in patients was 1798.5 IU/L. Other demographic variables including time from poisoning to hospital, systolic and diastolic blood pressure, GCS, Initial atropine dose, Duration of hospitalization and ventilation have been shown in (Table

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Table 1: Comparison of mortality and survival between two groups of study

PR prolongation	Death (%)	Live (%)	Total
yes	3 (33.3)	6 (66.6)	9
no	13 (7.1)	169 (92.9)	182
Total	16 (8.4)	175 (91.6)	191

Table 2: Various types of organophosphates

Organophosphate type, chemical or trade name	**N (%)**
Diazinon	31 (15.5)
Malathion	15 (7.5)
Chlorpyrifos	6 (3)
Cyhalotrine	1 (0.5)
Zolone	1 (0.5)
Gusathion	1 (0.5)
Oxydemeton methyl	5 (2.5)
Pyrymphous methyl	1 (0.5)
Ethion	1 (0.5)
Bichon	1 (0.5)
Guthion (azinphos_methyl)	1 (0.5)

3). Deaths occurred in 16 (7.9%) patients, from whom 3 patients had conductive abnormality (PR prolongation) in ECG.

There was no significant difference from the point of respiratory failure and systolic blood pressure<90mm Hg between two groups of our study (prolonged and normal PR intervals) (p=0.96 andp=0.38) (Table 4).

The mortality rate in the long PR group was significantly higher than that of the normal

Table 3: Demographic data

Variables	**(mean ± SD)**
Time from poisoning to hospital, hour	6.5±16
Butyrylcholinesterase, lowest, U/L	1798±2572
Systolic blood pressure, mmHg	114±24.5
Diastolic blood pressure, mmHg	71±16.5
GCS (mean, Min and Max) (13, 3 and 15)	
Initial atropine dose (mg)	7.41±13.36
Duration of hospitalization (mean, Min and Max)day	7, 1 and 30
Duration of ventilation (mean, Min and Max) day	7.1, 1 and 29

Table 4: Comparison of respiratory failure and SBP between two groups of study

PR prolongation	**With Respiratory failure (%)**	**Without respiratory failure (%)**	**SBP ≤ 90**
Yes	3 (33.3)	6 (66.7)	0 (0)
No	62 (34.1)	120 (65.9)	14 (7.7)

Table 5: Comparison of mortality between two groups of study

	PR prolongation (%)	**NO PR prolongation (%)**
Mortality	3 (33.3)	13(7.1)

P value: 0.014

PR group (P=0.014) (Table 5). Moreover, the average period of hospitalization in patients with prolonged interval was not higher than the other group (P=0.76). There was no significant difference between Atropine approval and mortality (P=0.94). Undesirable outcome including death, vegetative state, CPR, blood transfusion and intermediate syndrome wasseen in 6 (33.3%) patients with PR prolongation and 21 (11.5%) in patients without prolongation. From 201 patients, 180 (89.6%) had received atropine, this variable was not related with mortality (P value>0.05). In our study we considered some variable as a bad outcome including (death, vegetative state, CPR, blood transfusion and intermediate syndrome). They were seen in 6 (33.3%) patients with PR prolongation and 21

(11.5%) in patients without prolongation. PR prolongation did not predict them (P value=0.07).

4. Discussion:

The ECG may display a variety of abnormalities in acute organosphate poisoning. Classically, cardiac rhythm in organophosphate poisoning consists of two phases: a transient phase of intense sympathetic tone, causing sinus tachycardia, followed by a second phase of extreme parasympathetic tone, causing sinus bradycardia, atrioventricular block, and ST segment and T wave abnormalities (7).

ECG changes are prolonged QTc interval, ST segment elevation, low-amplitude Twaves, extrasystole and prolonged PR interval (8).

Prolongation of the electrocardiographic PR interval, conventionally known as first-degree atrioventricular block (AVB) when the PR interval exceeds 200 milliseconds, is frequently encountered in clinical practice (9).

The mechanism of cardiac toxicity induced by OP compounds is unclear. A direct toxic effect on the heart, unrelated to deficient acetylcholinesterase activity and uninfluenced by atropine administration, has been postulated. This effect may be dose related automaticity refers to a cardiac muscle cell firing off an impulse on its own. All of the cells in the heart have the ability to initiate an action potential; however, only some of these cells are designed to routinely trigger heart beats. These cells are found in the conduction system of the heart and include the SA node, AV node, bundle of His, and Purkinje fibres (10).

Based on our results, PR prolongation more than 2 second was seen in 9 (4.7%) patients. Several studies have evaluated the electrocardiographic findings associated with organophosphate poisoning. Gul EE, evaluated a group of 36 patients with organophosphate poisoning. Variety of ECG abnormalities was identified as follow: sinustachycardia in (72%), sinus bradycardia in (11%), 1st-degree AV block in (6%), right bundle branch block in (6%), ST–Tchanges in (19%), and prolongation of the QT interval in (19%) of patients (11).

Karki *et al* reported ECG abnormalities including prolonged Q-Tc interval in 14 cases (37.8 percent), ST-T changes in 11 cases (29.7%), and conduction defects in two cases (5.4%) (12).

Vijayakumar *et al.* reported that ECG analysis, including rate, ST-Tabnormalities, conduction defects, and measurement of PRand ‘‘QTc’’ intervals and PR prolongation was absent in both men and women (8).

Saadeh A *et al* reported cardiac arrhythmias in 20 (43%), electrocardiographic abnormalities including prolonged Q-Tc interval in 11 (24%), ST-T changes in 31 (67%), and conduction defects (PR prolongation in 2 man and 2 woman) in 4 (9%) (13).

Rahbar Taromsari M. *et al* reported Sinus tachycardia with (31%) as the most common ECG abnormality. Non-specific ST-T changes were seen in (24%) and Conduction disturbances were seen 15 (20 %) in men and 2 (8%) in women with total of 17 (17%). Overall, mortality rate was 5% and all of the deceased patients presented changes in ECG (1).

5. Conclusion:

In our study it has been well demonstrated that PR-interval prolongation affects mortality rate. Patients with PR prolongation had more undesirable outcome (death+ vegetative state, CPR, blood transfusion, intermediate syndrome) than patients without PR prolongation. PR prolongation indicates poor prognosis. Careful observation of the electrocardiogram of the patients exposed to OP compounds is necessary, parallel to the appropriate medical treatment.

Acknowledgments

We would like to thank all ED personnel who helped in diagnosis and management of this patient.

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