Evaluation of Cardiac Effect in Acute Organophosphate Poisoning

Mehmet Yüzügüllü  
TC Sağlık Bakanlığı: Türkiye Cumhuriyeti Sağlık Bakanlığı

Zeynep Kekeç  
Çukurova Üniversitesi Tıp Fakültesi: Çukurova Üniversitesi Tıp Fakultesi

Didem Yüzügüllü (didemata8@gmail.com)  
Türkiye Cumhuriyeti Sağlık Bakanlığı: Türkiye Cumhuriyeti Sağlık Bakanlığı  
https://orcid.org/0000-0001-6731-6155

Research Article

Keywords: cardiac effect, organophosphate poisoning, pseudocholinesterase, toxicology

Posted Date: January 23rd, 2023

DOI: https://doi.org/10.21203/rs.3.rs-2498267/v1

License: ☛ This work is licensed under a Creative Commons Attribution 4.0 International License.  
Read Full License
Abstract

Aim

The aim of this study is to investigate the cardiac effects in acute organophosphate poisonings with the emergency approach.

Material and Methods

Patients over the age of 15 with cholinergic toxic syndrome symptoms who applied to the Emergency Medicine Department due to organophosphate poisoning were prospectively included in the study. The type and level of organophosphate were analyzed. Creatine kinase, creatine kinase MB isoenzyme, troponin T, pseudochoolinesterase were measured. Rhythm, rate, PR distance, corrected QT interval, ST-T changes, right and left bundle branch block, right and left axis deviation were evaluated in ECG.

Results

Forty-six patients (27 female, 19 male), were included in the study. The 6th hour creatine kinase, creatine kinase MB and Troponin T values of the patients were significantly higher than values at the time of admission. A positive and statistically significant correlation was found between the creatine kinase values at the time of admission and the pseudochoolinesterase values of the patients. A positive correlation was found between creatine kinase -MB and pseudochoolinesterase values at the time of admission. Similarly, a positive correlation was found between Troponin-T and pseudochoolinesterase. After taking Diazinon, Chlorpyrifos and Cypermethrin, sinus tachycardia was observed at the time of admission. After carbofuran intake, the ECG rhythm at admission was normal, and sinus tachycardia was observed at the 6th hour. It was determined that the QT interval was long at the time of admission after taking Chlorpyrifos. After diazinon and cypermethrin intake, the QT interval was evaluated as long at the 6th hour. Left bundle branch block was observed after cypermethrin intake.

Conclusion

Organophosphate compounds are one of the important causes of poisoning. The results of this study, which examines cardiac enzymes and ECG changes after organophosphate poisoning, will provide important contributions to the literature.

Introduction

Organophosphate insecticides have been widely used all over the world since the 1970s for the protection of vegetables, fruits and other agricultural products. Çukurova region, which includes Adana, is the region where agriculture is most common in our country. Therefore, pesticides are used more intensively but
unconsciously in this region [1]. Organophosphate poisoning is an important preventable health problem in developing countries. Although there are accidental poisonings by exposure or inhalation, serious poisonings usually occur after suicidal ingestion [2]. A high rate of death has been reported in the past, attributed to delayed diagnosis and malpractice [3].

About three million people are exposed to organophosphates a year, and nearly 300,000 die. They are highly toxic and can be life threatening. The most common cause of poisoning is accidental and suicidal ingestion. Apart from these, poisoning may occur by consuming contaminated food and beverages and wearing contaminated clothing [4]. It is one of the common causes of poisoning, especially in developing countries such as Turkey. Acute poisoning occurs with cholinergic system findings. The autonomic nervous system, neuromuscular junction and central nervous system are most commonly affected. In case of ingestion of fast-acting agents, respiratory arrest or cardiogenic shock may occur within 30 minutes. Before reaching the hospital, death may occur. Blurring of consciousness, coma, convulsions, fasciculations, muscle weakness, tachycardia, hypertension, bronchospasm, salivation, myosis can be seen as clinical findings, and these may occur at different times. Routine laboratory tests are not diagnostic, but there may be signs of pancreatitis, hypo/hyperglycemia, and abnormal liver function tests. The electrocardiography (ECG) may be abnormal; it correlates with the degree of toxicity and ventricular dysrhythmias, torsades de pointes may occur. Heart blocks and prolongation of the QT interval are common [5].

Organophosphate insecticides inhibit acetylcholinesterase (AChE) and cholinesterase enzymes, which cause hyperstimulation at the cholinergic junction [6]. The differences in clinical course are based on the properties of different organophosphate insecticides and their AChE-lowering effects [7, 8]. As it is known, hereditary deficiency, liver failure, malnutrition, cocaine, codeine, iron deficiency anemia, serum cholinesterase, which is stimulated by drugs such as morphine and succilincholine, shows high variability; which makes this enzyme a good-for-bad marker in organophosphate poisoning if the previous blood level is unknown [9].

The aim of this study is to investigate the cardiac effects in acute organophosphate poisonings and to determine its contribution to the emergency approach and to guide future studies in order to prevent possible complications due to organophosphate poisoning and to reduce death and disability.

**Material And Methods**

The necessary permission was obtained from the ethics committee of Çukurova University Faculty of Medicine (meeting numbered - decision numbered 1). Patients over the age of 15 with cholinergic toxic syndrome symptoms who applied to the Emergency Medicine Department due to organophosphate poisoning or pesticide intake were prospectively included in the study. After the informed consent form was read to the patients and their consent was obtained, age, gender, presence of additional disease status, route of ingestion of the toxin, and patient data were recorded in the study form prepared in
advance. At the time of admission, before starting antidote treatment, blood samples were taken to determine the level and type of organophosphate.

**Measurement Of Serum Organophosphate Levels**

Analyzes of the type and level of organophosphate were performed in the Forensic Toxicology laboratory. Blood samples were prepared using the solid-liquid extraction method. Extracted samples were analyzed with Agilent brand 6890 Gas Chromatograph (GC) and 5973 Mass Spectrometry (MS) instrument. GC/MS was run in the selected ion mode. Concentrations were measured by preparing calibration curves with certified pesticide standard substances. Pesticide concentrations were calculated at mg/l (ppm).

**Biochemical Studies**

Measurements of blood samples were made in Çukurova University Faculty of Medicine Balcalı Hospital central laboratory.

**Creatine Kinase (CK)**

It was measured by 'Enzymatic Calorimetric Test' method at 2–8˚C in serum with Integre Cobas biochemical analyzer. The normal value in serum was 26–140 U/L.

**Creatine kinase MB isoenzyme (CK-MB)**

Measurement was made with Elecsys 1010/1020 and modular analytical (Elecsys module) immunoassay analyzer method. The normal value in serum was 0.94–4.94 ng/ml.

**Troponin T**

Measurement was made with ECLIA (Electrochemiluminescence Immunoassay) roche elecsys 1010 and 1020 immunoassay analysis. The normal value in serum was < 0.1 ng/ml.

**Pseudokolinesterase (PKE)**

Measurements were made with the Roche Cobe Integra 800 device using the S-butyryltiocholine iodide method. Its normal value was 3930–10800 IU/L.

**Electrocardiographic Evaluation**

Rhythm, velocity, PR interval, corrected QT interval, ST-T changes, right bundle branch block, left bundle branch block, right axis deviation, and left axis deviation were evaluated in the ECG taken with the Philips PageWriter Trim III ECG device. Cardiac rhythm was evaluated by grouping it as normal sinus rhythm, sinus tachycardia, sinus bradycardia and other rhythm disorders. PR distance was measured from the
beginning of P to the beginning of R on the ECG trace. The normal value was accepted as 0.12–0.20 sec. Corrected QT distance was calculated using the QT/ √R-R formula. The normal range was determined as 0.36–0.44 sec.

Statistical analysis

SPSS 24.0 package program was used for statistical evaluation of the data. Categorical measurements were evaluated as numbers and percentages, and numerical measurements as mean and standard deviation (median and minimum-maximum where necessary). Chi-square test was used to compare categorical measures between groups. T Test was used in the analysis of continuous variables. Statistically, p < 0.05 was considered significant.

Results

Forty-six patients over the age of 15, 27 (58.7%) female and 19 (41.3%) male, were included in the study. The mean age of the patients was calculated as 34.4 ± 12.7 years. At the time of first admission to the emergency department, 3 (6.7%) patients needed mechanical ventilators due to impaired consciousness or respiratory failure. Forty-three (93.3%) patients did not need mechanical ventilators. The mean hospitalization period of the patients was calculated as 3.69 ± 1.15 days. While 91.3% of poisonings were by mouth for suicidal purposes, 8.7% occurred after accidental exposure. 100% of the patients were discharged with cure.

Among the patients, 1 (2.2%) was Diazinon, 1 (2.2%) Chlorpyrifos, 1 (2.2%) Cypermethrin, 1 (2.2%) Fenitratrin, 1 (2.2%) was poisoned with Carbofuran. Although 41 patients (89.1%) had clinical signs of cholinergic poisoning, the pesticide type that caused the cholinergic toxidrome finding could not be determined, since no toxic factor could be detected in the laboratory. Diabetes Mellitus (DM) disease was present in 1 (2.2%) of the cases. Other patients (n:45; 97.8%) did not have any comorbidity known before.

Pseudocholinesterase (PChE) values of the patients at admission were normal in 11 (23.9%) patients and low in 35 (76.1%) patients. Sixth hour PChE values were normal in 17 (37.0%) patients and low in 29 (63.0%) patients. Twelfth hour PChE values were normal in 23 (50.0%) patients and low in 23 (50.0%) patients. There was a statistically significant correlation between admission and 6th hour PChE values (p < 0.050). In addition, there was a statistically significant correlation between 6th hour and 12th hour PChE values (p < 0.050). The 6th hour CK, CK-MB and Troponin T values of the patients were significantly higher than the CK, CK-MB and Troponin-T values at the time of admission (Table 1).
A positive and statistically significant correlation was found between the CK values at the time of admission and the PChE values of the patients (p = 0.020). A positive and statistically significant correlation was found between CK-MB and PChE values at the time of admission (p = 0.031). Similarly, a positive and statistically significant correlation was found between Troponin-T and PChE values at the time of admission (p = 0.038) (Table 2).
Table 2
Evaluation of Cardiac Enzymes and Pseudocholinesterase Serum Levels of Arrival, 6th Hour and 12th Hour Measurements by Pearson Correlation Test

<table>
<thead>
<tr>
<th></th>
<th>Pearson Korrelation</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 hour CK - Pseudocholinesterase</td>
<td>0.341</td>
<td>0.020</td>
</tr>
<tr>
<td>6th hour CK - Pseudocholinesterase</td>
<td>0.016</td>
<td>0.916</td>
</tr>
<tr>
<td>12th hour CK - Pseudocholinesterase</td>
<td>0.185</td>
<td>0.219</td>
</tr>
<tr>
<td>0 hour CKMB - Pseudocholinesterase</td>
<td>0.318</td>
<td>0.031</td>
</tr>
<tr>
<td>6th hour CKMB - Pseudocholinesterase</td>
<td>0.170</td>
<td>0.259</td>
</tr>
<tr>
<td>12th hour CKMB - Pseudocholinesterase</td>
<td>0.155</td>
<td>0.304</td>
</tr>
<tr>
<td>0 hour Troponin - Pseudocholinesterase</td>
<td>0.306</td>
<td>0.038</td>
</tr>
<tr>
<td>6th hour Troponin - Pseudocholinesterase</td>
<td>0.094</td>
<td>0.536</td>
</tr>
</tbody>
</table>

The ECG findings of the patients were evaluated according to the pesticide type. After taking Diazinon, Chlorpyrifos and Cypermethrin, sinus tachycardia was observed in the ECGs of the patients at the time of admission. After carbofuran intake, the ECG rhythm at admission was normal, and sinus tachycardia was observed at the 6th hour. In the ECG evaluation, it was observed that the PR distance for all pesticides was within the normal range. It was determined that the QT interval was long at the time of admission, and returned to the normal range at the 12th hour after taking Chlorpyrifos. After diazinon and cypermethrin intake, the QT interval was within the normal range at the time of admission, it was evaluated as long at the 6th hour and normal at the 12th hour. However, left bundle branch block was observed as an ECG finding after cypermethrin intake (Table 3). Regardless of the pesticide type, the ECG rhythm evaluations of all participants at the time of application, at the 6th hour and at the 12th hour are given in Fig. 1.
Table 3
ECG Findings of Patients with Pesticide Detected in Toxicology Analysis

<table>
<thead>
<tr>
<th></th>
<th>Diazinon</th>
<th>Chlorpyrifos</th>
<th>Cypermethrin</th>
<th>Fenitrothion</th>
<th>Carbofuran</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 hour ECG Rhythm</td>
<td>Sinus Tachycardia</td>
<td>Sinus Tachycardia</td>
<td>Sinus Tachycardia</td>
<td>Normal Sinus Rhythm</td>
<td>Normal Sinus Rhythm</td>
</tr>
<tr>
<td>0 hour QT interval</td>
<td>Normal</td>
<td>Long</td>
<td>Normal</td>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td>0 hour PR distance</td>
<td>Normal</td>
<td>Normal</td>
<td>Normal</td>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td>6th hour ECG Rhythm</td>
<td>Sinus Tachycardia</td>
<td>Sinus Tachycardia</td>
<td>Sinus Tachycardia</td>
<td>Normal Sinus Rhythm</td>
<td>Sinus Tachycardia</td>
</tr>
<tr>
<td>6th hour QT interval</td>
<td>Long</td>
<td>Long</td>
<td>Long</td>
<td>Short</td>
<td>Normal</td>
</tr>
<tr>
<td>6th hour PR distance</td>
<td>Normal</td>
<td>Normal</td>
<td>Normal</td>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td>12th hour EKG Rhythm</td>
<td>Normal Sinus Rhythm</td>
<td>Sinus Tachycardia</td>
<td>Sinus Tachycardia</td>
<td>Normal Sinus Rhythm</td>
<td>Sinus Tachycardia</td>
</tr>
<tr>
<td>12th hour QT interval</td>
<td>Normal</td>
<td>Normal</td>
<td>Normal</td>
<td>Short</td>
<td>Normal</td>
</tr>
<tr>
<td>12th hour PR distance</td>
<td>Normal</td>
<td>Normal</td>
<td>Normal</td>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td>ECG</td>
<td>Normal Sinus Rhythm</td>
<td>Normal Sinus Rhythm</td>
<td>Left Branch Block</td>
<td>Normal Sinus Rhythm</td>
<td>Normal Sinus Rhythm</td>
</tr>
</tbody>
</table>

Discussion

Organophosphate compounds are widely used all over the world. It is one of the most common causes of poisoning, especially in developing countries such as Turkey. Poisoning is common among agricultural workers and children [10]. In the Çukurova region, where agriculture is at the forefront, easy access to pesticides increases the rates of poisoning. Admissions to the emergency department of our hospital, which is a large regional hospital, are encountered at a high rate, especially due to cholinergic toxidroma due to organophosphate compounds. In a study conducted at Çukurova University Faculty of Medicine, it was determined that 23.9% of poisoning patients who applied to the emergency medicine service between 1997 and 2006 were organophosphate poisoning [11].

Organophosphate compounds can be rapidly absorbed from the skin, mucous membranes, gastrointestinal tract, eyes and respiratory tract. Organophosphate compounds are distributed and accumulated in adipose tissue, liver and kidneys. Phosphothioates (P = S) are more lipophilic than phosphates (P = O). Therefore, they show more accumulation in adipose tissue. Since they are stored in
the adipose tissue, their removal from the organism is slow and may take a few days in more lipophilic ones [10, 12].

Organophosphate compounds inhibit AChE and cholinesterase enzymes, causing hyperstimulation at the cholinergic junction [4]. Although serum cholinesterase is a frequently used marker, it is actually high due to hereditary deficiency, liver failure, malnutrition, iron deficiency anemia, drugs such as cocaine, morphine, codeine, and succinylcholine. varies. Therefore, if its historical level is unknown, only the best of worst makes this enzyme a marker in organophosphate poisoning [9].

Serum and erythrocyte acetylcholinesterase measurements are the most widely used methods in practice. Since erythrocyte acetylcholinesterase is found in skeletal muscle and nervous tissue, the measurement result also reflects acetylcholinesterase enzyme activity in peripheral tissue, brain and muscle. However, although erythrocyte acetylcholinesterase measurements are more specific in the detection of organophosphate poisoning, serum acetylcholinesterase measurements are more preferred due to the ease and accessibility of measurement. Since serum acetylcholinesterase activity in the population shows individual differences, it is accepted that it is more accurate to determine the decrease or increase in serum acetylcholinesterase activity instead of a reference range in the evaluation of the response given as a result of treatment. Clinically, changes in the direction of decreased acetylcholinesterase activity are important. It proves that the exposed substance has anticholinesterase properties and gives an idea of the degree of inhibition [13].

Studies have reported that serum cholinesterase tests can be helpful in the diagnosis of OP poisoning and can be used as a guide to evaluate the clinical course of poisoning [14]. Aygün et al. [15] reported that very low cholinesterase levels support the diagnosis of acute OP poisoning and show a poor clinical course. Tang et al. [16] reported the association of serum cholinesterase with clinical severity. Of the 46 patients included in the study, 35 (76.1%) had low pseudocholinesterase values at presentation. This result is similar to previous studies and when evaluated together with clinical findings, we can say that it supports the diagnosis of organophosphate poisoning. The 6th hour PChE value was low in 63% of the patients, and the 12th hour PChE value was low in 50% of the patients. A significant decrease was observed.

CK, CK-MB and Troponin T values were found to be elevated at the 6th hour compared to the time of admission. It was observed that there was a positive correlation between CK and PChE values at the time of admission, between CK-MB and PChE values, and between Troponin T and PChE values. However, there is no significant correlation between the values measured at the 6th hour and the 12th hour. In studies examining the clinical effects observed after organophosphate poisoning, it was reported that bradycardia was first observed due to muscarinic effects on heart tissue, and ventricular dysrhythmias may also occur. It has been stated that tachycardia and hypertension may also be observed in more severe poisonings due to nicotinic effects. In these studies, it has been shown that acute fenthion poisoning causes myocardial damage [17, 18]. After exposure to organophosphate compounds, signs of poisoning are generally observed within 30 minutes to 3 hours [19]. After ingestion of serious amounts by
mouth, symptoms may begin in the 5th minute and death may occur in the 15th minute, while a small amount of skin exposure may cause mild complaints. What is generally seen is that almost all cases become symptomatic in the first 24 hours, mostly in the first 8 hours. They cause bradycardia as a result of indirect muscarinic effect and stimulation of parasympathetic ganglia [20].

It is noteworthy that different ECG changes are observed for different pesticide types. In addition, it was observed that the percentage of participants with normal sinus rhythm decreased at the 6th hour compared to the time of arrival, but increased again at the 12th hour. The most common cardiac findings following poisoning are a decrease in blood pressure and a decrease in heart rate. Patients rarely experience increased heart rate and blood pressure due to nicotinic receptor stimulation. Cardiac manifestations are often the cause of serious problems and death. Electrocardiographic findings are prolonged Q-T interval, ST segment elevation, T wave depression and prolonged PR time. It may be in abnormal rhythms such as sinus bradycardia, ventricular extrasystole, ventricular tachycardia, and fibrillation [19].

Organophosphate compounds are one of the important causes of poisoning. Its clinical effects depend on the accumulation of acetylcholine in cholinergic junctions, central nervous system, muscle-nerve junctions and autonomic ganglia. They are highly toxic and can be life threatening. When the studies in the literature were examined, it was seen that cardiac enzymes and ECG changes after organophosphate poisoning were not examined in detail as in our study. Therefore, the results of the study will have important contributions.

Declarations

The Authors declare that there is no conflict of interest.

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Ethical approval for this study was obtained from the ethics committee of Çukurova University Faculty of Medicine (Meeting No.3, date December 23, 2010, – Decision No. 1).

The authors declare that no funds, grants, or other support were received during the preparation of this manuscript.

All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by Mehmet Yüzügüllü, Zeynep Kekeç and Didem Yüzügüllü. The first draft of the manuscript was written by Mehmet Yüzügüllü and Didem Yüzügüllü and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Informed consent was obtained from all individual participants included in the study.
References


Journal of Emergency Medicine 37(9), 1611-1617.


**Figures**

![Figure 1](image-url)

---

**Figure 1**
ECG Rhythm Evaluations of Participants at the Time of Application to the Emergency Department and After