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Original Research Paper

General Medicine

CARDIOVASCULAR MANIFESTATIONS IN ACUTE ORGANOPHOSPHATE POISONING

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ABSTRACT Organophosphorus poisoning is a significant health concern, particularly in developing countries. This study aimed to investigate the cardiac manifestations of organophosphorus compound ingestion and explore the frequency and variation of electrocardiogram (ECG) and 2D-echocardiography changes in patients with organophosphorus poisoning. The study included 50 patients admitted to Shadan Institute of Medical Sciences between 2021 and 2023. The results showed that 62% of the patients had electrical abnormalities recorded on ECG, while 38% had no abnormalities. Sinus tachycardia was the most common abnormality, followed by ventricular premature complexes, sinus bradycardia, and atrial fibrillation. Additionally, 22% of the patients exhibited echocardiographic abnormalities. The study highlights the prevalence of cardiovascular abnormalities in organophosphorus poisoning and emphasizes the need for further research on the correlation between ECG and echocardiographic changes in these patients. Understanding the cardiac manifestations of organophosphorus poisoning is crucial for effective management and treatment strategies.

KEYWORDS :

INTRODUCTION

India being a predominantly agricultural country, pesticides are freely, and easily available, and organophosphorus poisoning is a major health issue (1). Pesticide use in India began in 1948, when DDT was introduced to control malaria mosquitoes and benzene hexachloride to control locusts, and these substances and numerous others have since been produced in the country. Increased pesticide use in agriculture has increased the quality and quantity of Indian food production. However, there has been an increase in the use of these products for deliberate self-harm and suicide attempts; indeed, intentional poisoning is more common than accidental poisoning (2).

Acute Organophosphorus poisoning (OP) is widespread in the developing world and its frequency is increasing. WHO has estimated that nearly 2, 00,000 people worldwide die from pesticide poisoning. In India also it is the commonest poisoning and exposure to OP compounds in the form of nerve agents and pesticides poses an ever increasing military and civilian threat (3). The number of intoxications with OPs is estimated at some 3,000,000 per year, and more than 80% of them are pesticide-related hospitalizations. The total fatality rate has been estimated at 20% (3).

The easy availability of toxic pesticides such as OPs that are used in agriculture has made pesticides as the agents of choice for self-harm. The extent of acute pesticide poisoning in agricultural workers, particularly in developing countries, has often been estimated on inadequate information. This information has resulted in global estimates and regional, localized, or field assessments. The used methods include descriptive epidemiology, cross-sectional and case studies. Extrapolations and assumptions to estimate global pesticide poisonings have often been based on chemical-related fatalities in a small number of countries. Therefore, such estimates do not provide reliable data (4). Many reports do not adequately distinguish between intentional, accidental, and occupational pesticide poisoning statistics or are dominated by cases of intentional (suicidal) poisoning which, by their nature, result in severe toxicity with high mortalities. The majority of reports do not adequately describe whether individual cases are mild, moderate, or severe poisoning. Occupational acute pesticide poisonings in developing countries are a small proportion of overall reported poisoning and are associated with the more minor effects of pesticides exposure (5).

Cardiac Manifestations of Organophosphorus poisoning

ECG changes associated with Organophosphorus compound ingestion have been studied in the past (9,10,11) and a varying number of electrical changes been observed and work on these ECG manifestations has been published. As observed the most common ECG manifestation of Organophosphorus compound poisoning was a prolonged QTc interval, followed by sinus bradycardia/tachycardia and ST-T changes including ST elevations/depressions and T wave inversions. Other findings also include ventricular arrhythmias, atrial fibrillation and prolonged PR interval (10).

AIMS AND OBJECTIVES OF THE STUDY

- To study the occurrence of signs and symptoms in organophosphate poisoning
- To Study the Cardiovascular Manifestations in Acute Organophosphate Poisoning
- To determine the frequency and variation of ECG changes in organophosphate poisoning.
- To determine the frequency and variation of 2D-ECHO changes in organophosphate poisoning

Basic Structure of Organophosphorus Compound

All OP compounds share a similar chemical structure. Their central component is a phosphorous atom with a double bond to either oxygen (P = O) or sulphur (P = S), and three side chains. One side chain, the X group or leaving group, differs widely between the OP agents and determines many of its physical and chemical characteristics. The two other side chains, the R1 and R2 groups, are typically alkoxy groups but can be almost any aliphatic or aromatic hydrocarbon.

These side chains also differ between individuals OP agents and account for some Variability in their toxicokinetics. Compounds with a sulphur atom (P = S) instead of an oxygen atom (P = O) bound to the phosphorus core are known as phosphorothioates or organothiophosphorus compounds(6).

OP compounds are either solids or liquids. Solid compounds may be applied as powders when used as an insecticide, but more commonly they are dissolved in a liquid hydrocarbon vehicle for application. Most commercially available OP products are therefore oily liquids. Whereas some are odorless, many are described as having a garlic-like or kerosene odor of varying strength. Most OP compounds decompose rapidly in the environment by photolysis or

hydrolysis.

Commercial agricultural OP products have a high toxicity. Animal and household OP products are typically much less potent. An agent's relative toxicity is generally expressed as a measurement of its lethal dose in experimental animals (LD50) (6)

Mode Of Intoxication

Exposure to OP insecticides can occur by almost any route. Occupational exposures generally occur via direct dermal or mucous membrane contact or by inhalation. Most OP insecticides are not volatile, so exposure by the respiratory route is generally the result of inhalation of aerosolized droplets. Occasionally, accidental exposures may occur with ingestion of contaminated foodstuffs. Intentional (e.g., suicide) exposures are typically ingestions or parenteral injections of OP compounds. Most OP compounds are extremely lipophilic. They are therefore readily absorbed by passive diffusion across lung and gastrointestinal system or skin. Deliberate ingestion is common with suicidal intension in developing countries, where they are readily available and cheap (7).

Pathophysiology And Clinical Manifestations

OP compounds are cholinesterase inhibitors and exert their toxicity by interfering with the normal function of acetylcholine, an essential neurotransmitter throughout the autonomic and central nervous system. Organophosphates are powerful inhibitors of carboxylic ester hydrolases including chymotrypsin, acetylcholinesterase, plasma or butyrlcholinesterase (pseudocholinesterase), plasma and hepatic carboxylesterases (aliesterases), paraoxonases (A-esterases), and other nonspecific proteases (8).

Although organophosphorous compounds differ structurally from acetylcholine, they can bind to the acetylcholinesterase molecule at the active site and phosphorylate / phosphonate the serine moiety. When this occurs, the resultant conjugate is infinitely more stable than the acetylcholine- acetylcho linesterase conjugate, although endogenous hydrolysis does occur (8,9).

Clinical Features

In most of the instance's symptoms appear within 30 minutes of exposure and usually in less than 12hrs and almost always in less than 24hrs. Therefore, symptoms which begin more than 24 hrs after exposure cannot be attributed directly to acute organophosphate poisoning.

Poisoning typically represents a dynamic mixture or balance of both muscarinic and nicotinic systems. GI symptoms appear first before the onset of systemic symptoms. The local effect of OP exposure on the eye and the respiratory tract are immediate. The ocular effects are miosis, conjunctival hyperemia, heaviness in and behind the eyes and dimness of vision. The respiratory manifestations are rhinorrhea nasal hyperemia, tightness in chest and occasionally prolonged expiration and increased bronchial secretion. Acute toxicity typically occurs after a single exposure when a significant threshold level of cholinesterase inhibition has been reached.

Tachycardia and increased blood pressure occurs in initial stage and Bradycardia and low blood pressure in the later stage. Commonest effect observed was tachycardia. Late onset bradycardia is attributed to direct action on myocardium by organophosphorus compound. Hypertension occurs due to the combined effect of vasoconstriction from cholinergic stimulation of sympathetic ganglia and noradrenaline release from adrenal medulla. Hypotension may also occur due to muscarinic action or blocking of ganglia by hyperpolarization. Cardiac manifestations including atrial fibrillation, conduction block and ventricular fibrillation and further usually occur in terminal stages. ECG changes seen were sinus bradycardia, right axis deviation, AV Block, ST segment depression in all leads and T wave inversion. A combination of metabolic and electrolyte derangements cause myocardial injury, autonomic dysfunction and asynchronous repolarization producing variable QRS morphology and varying RR interval (10,11).

METHODOLOGY

Patients and Methods

The study population comprises of 50 cases who were admitted in the Department of General Medicine, Shadan institute of medical sciences, Hyderabad, with history and clinical features suggestive of organophosphate poisoning. The study period was from June 2021 to June 2023. Patient or patient's attendant consent was taken and ethical clearance was obtained from the Institute's Ethical Committee.

Type of study:

Cross sectional study

Sampling:

Convenient sampling

Criteria for selection of study group:

Inclusion Criteria:

All patients admitted to Shadan Institute of Medical Sciences due to alleged ingestion of Organophosphate poisoning between June 2021 and June 2023.

Exclusion Criteria:

Any patients with a history of previously diagnosed cardiovascular disorders.

Variables and measurement:

Independent variable

ECG: A 12 lead ECG will be taken on presentation

- Normal ECG
- AF
- Conduction abnormalities
- Rate abnormalities
- Bundle branch blocks
- Rhythm changes (Bradycardia, Tachycardia)
- ST-T segment changes
- T wave changes

2D ECHO:

Transthoracic echocardiogram will be used.

- Motion wall abnormalities
- Systolic Dysfunction
- Diastolic Dysfunction

Dependent variable

Confirmed Cases of organophosphate poisoning Based on

- Clinical features
- History

Data entry and Statistical Analysis

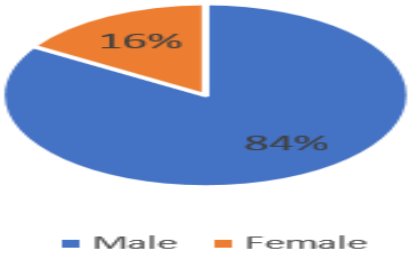
Data was entered into Microsoft Excel sheet and analyzed using IBM SPSS Statistics for Windows, Version 22.0.

Descriptive statistics were expressed as Means and percentages

- Data was entered into Microsoft Excel sheet and analyzed using IBM SPSS Statistics for Windows, Version 22.0.
- Descriptive statistics were expressed as Means and percentages
- Inferential statistical analysis was done using chi-square tests, and one sample binomial non parametric tests.
- P-value of <0.05 will be considered statistically significant
- The majority of the cases admitted in this study population

- were male (84%) with 42 of the 50 admitted cases and females were (16%) with 8 of the fifty cases.

OBSERVATIONS AND RESULTS



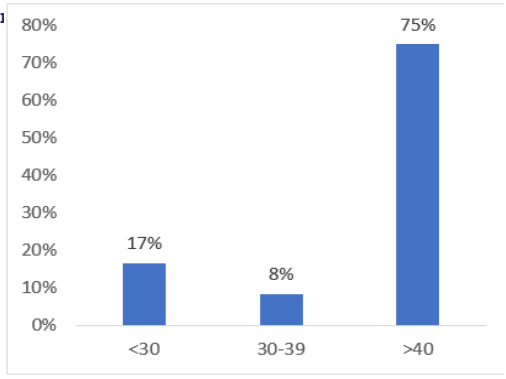


Figure-2: Age Distribution

Table 1: ECG Changes in the Study Population

ECG Changes	n	Percentage (%)
Prolonged QT interval/QTc	10	20
Prolonged PR Interval	3	6
T inversion	5	10
ST elevation	1	2
ST depression	2	4

- The most common ECG changes seen were a prolonged QTc interval and Sinus Tachycardia seen in 20% i.e. 10 of the 50 admitted cases.
- T inversions were the second most common, seen in 10% i.e. 5 of the fifty admitted cases.
- 6% of the cases presented with a prolonged PR interval.
- ST depression was present in 4% of the cases.
- 2% of the cases had ST elevation.

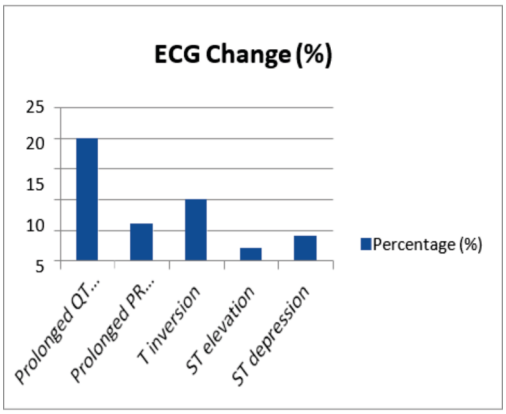


Figure 3: ECG Changes in the Study Population

Of the 50 patients we studied, 72% have no arrhythmias in the ECG. 20% of the patients have sinus tachycardia followed by VPCs in 4%, sinus bradycardia in 2%, and Atrial fibrillation in 2%. Of the 50 patients we studied, 92% have no heart blocks in the ECG. Left bundle branch block is seen in 6% of the patients and right bundle branch block in seen in 2% of study population.

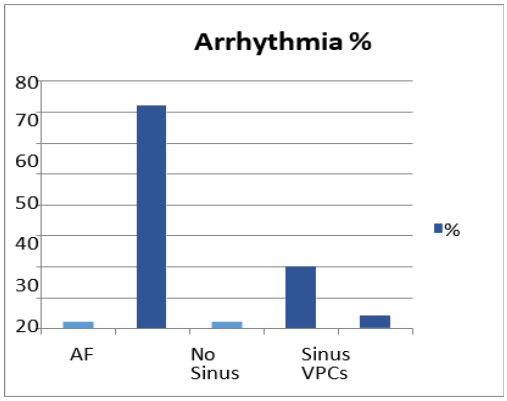


Figure 4: Arrhythmias in OP Poisoning

Table 2: ECG changes in OP Poisoning

ECG Changes	Frequency	Percentage (%)
No	19	38
Yes	31	62
Total	*50*	*100*

p- value: 0.120

Table 3: 2D ECHO Abnormalities in OP Poisoning

2D ECHO Changes	Frequency	Percentage (%)
No	39	78
Yes	11	22
Total	*50*	*100*

p- value: 0.000

Table 4: Cardiac Abnormalities in OP Poisoning

ECG Changes	Frequency	Percentage (%)
No	16	32
Yes	34	68
Total	*50*	*100*

p- value: 0.015

Of the fifty cases taken as a study population all of them received 2D Transthoracic Echocardiography once they were stabilized and their requirement for atropine intervention had reduced to insignificant levels or stopped.

- 20% of the cases (i.e. 10 cases) had Diastolic Dysfunction.
- 4% of the cases had systolic dysfunction.
- 2% of the cases had regional wall motion abnormalities.

The cardiac manifestations occur in a majority of affected patients and may range from innocuous electrocardiographic manifestations, such as sinus tachycardia, to life-threatening complications including cardiogenic pulmonary edema. Repolarization abnormalities, including ST segment elevation and T wave inversion as well as prolongation of the QTc interval, are among the most frequent cardiac manifestations of acute organophosphate poisoning. The mechanisms of organophosphate-induced cardiac toxicity are not fully understood. Aside from direct toxic effects of the organophosphate compounds, an increase in sympathetic and/or parasympathetic activity, hypoxemia, acidosis and electrolyte abnormalities are thought to be involved in myocardial damage associated with organophosphate poisoning.

Of the 50 patients we studied, 72% have no arrhythmias in the ECG. 20% of the patients have sinus tachycardia followed by VPCs in 4%, sinus bradycardia in 2%, and Atrial fibrillation in 2%.

Of the 50 cases taken as a study population for this study 8 had ECG changes that were confirmed to be cardiac abnormalities by further echocardiography.

16 of the 50 cases showed no abnormality recorded in either 2D- echocardiograph or by electrocardiogram. The calculated p-value of this study is 0.498 which shows that the presence of cardiac abnormalities in cases of Organophosphorous compound poisoning cannot be solely attributed to the toxic effects of the compound itself. There is no statistically significant difference between people who have ECG changes and who have 2D ECHO changes in OP poisoning patients with a p-value of 0.498 which is less >0.05.

CONCLUSION

This is a hospital based cross sectional point study done at Shadan Institute of Medical Sciences during the period of 2021-2023, which comprised of 50 patients who had ingested Organophosphorous compounds.The study population included 42 males and 8 females. Vomiting, salivation, sweating, lacrimation and excessive bowel movements are the most commonly presenting clinical features at the time of admission.

ECG abnormalities were seen in 30 of the 50 patients in this study i.e. 60% of the study population. QTc prolongation (20%) and sinus tachycardia (20%) were the most common abnormalities followed by T wave inversion (10%), BBB (8%), prolonged PR interval, ST segment depression (4%), ventricular arrhythmias (4%) and atrial fibrillation (2%), ST segment elevation (2%) and sinus bradycardia (2%). Of the 50 patients we studied, 92% have no heart blocks in the ECG. Left bundle branch block is seen in 6% of the patients and right bundle branch block in seen in 2% of study population. Of the 50 patients we studied, 72% have no arrhythmias in the ECG. 20% of the patients have sinus tachycardia followed by VPCs in 4%, sinus bradycardia in 2%, and Atrial fibrillation in 2%.

Echocardiographic abnormalities picked up by transthoracic 2D- Echocardiography were also present in 11 of 50 patients in this study i.e. 22% of the study population. The most common abnormality picked up on 2D-Echo was diastolic dysfunction (20%) of the cases followed by systolic dysfunction (4%). The least common change was regional wall motion abnormality (2%). There is a statistically significant difference between people who have 2D ECHO changes and who do not have 2D ECHO changes in OP poisoning patients with a p-value of 0.000 which is less <0.05. There is no statistically significant difference between people who have ECG changes and who have 2D ECHO changes in OP poisoning patients with a p-value of 0.498 which is less >0.05.

Currently, very limited data is available on echocardiographic abnormalities of OP poisoning. Further research is required on the echocardiographic changes in organophosphate poisoning patients and its correlation with the ECG abnormalities (11,12,13).

The organophosphate poisoning is associated with cardiac complications and most of them occur during the first few hours after exposure (14,15). Hypoxemia and electrolyte derangements are major predisposing factors for the development of these complications. Intensive supportive treatment, meticulous respiratory care and administration of atropine in adequate doses very early in the course of the illness are the keys to successful management of these cases. The estimated burden of organophosphate poisoning of 3,000,000 per year, demands a public health approach, availability and accessibility of health care services (16,17).

List Of Abbreviations Used

OP Organo Phosphorous ECG Electrocardiogram 2D-ECHO 2-Dimensional Echocardiograph ACETYL CoA Acetyl Co Enzyme A Ach Acetyl Choline Ache Acetyl Choline Esterase CNS Central Nervous System LD Lethal dose AV BLOCK Atrio Ventricular Block AF Atrial Fibrillation LBBB Left Bundle Branch Block LVH Left Ventricular Hypertrophy RBBB Right Bundle Branch Block VPC Ventricular Premature Complex QTc Corrected QT interval WHO World Health Organization

List Of Abbreviations Used

OP	Organo Phosphorous
ECG	Electrocardiogram
2D-ECHO	2-Dimensional Echocardiograph
ACETYL CoA	Acetyl Co Enzyme A
Ach	Acetyl Choline
Ache	Acetyl Choline Esterase
CNS	Central Nervous System
LD	Lethal dose
AV BLOCK	Atrio Ventricular Block
AF	Atrial Fibrillation
LBBB	Left Bundle Branch Block
LVH	Left Ventricular Hypertrophy
RBBB	Right Bundle Branch Block
VPC	Ventricular Premature Complex
QTc	Corrected QT interval
WHO	World Health Organization

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