

A Study of Cardiac Involvement in Organophosphorus Poisoning

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Abstract

Background and Objective: Organophosphorous (OP) poisoning frequently causes ill-health and death, particularly in developing countries. Not many clinical studies have been done to demonstrate the myocardial injury in OP poisoning through assessment of the cardiac biochemical markers. Hence, this is an attempt to study the myocardial injury in OP poisoning and to determine how it affects the outcome.

Materials and Methods: Patients with history of OP poison consumption who fulfil the inclusion and exclusion criteria, getting admitted. **Method of Collecting Data:** A total of 50 cases of OP poisoning meeting inclusion criteria of the present study have been studied.

Results: In this study, which included 50 patients of OP poisoning cases, tachycardia (30%) was the most common clinical sign seen, followed by bradycardia (20%), hypertension (16%), and hypotension (10%). The most common electrocardiographic abnormality seen was ST elevation (32%), followed by sinus tachycardia (30%), Q-T prolongation (24%), and sinus bradycardia (20%). Raised cardiac enzymes (troponin T and creatinine phosphokinase-MB [CK-MB]) were seen in 5 (10%) patients on the day 3. The levels of troponin T and CK-MB were elevated in patients with respiratory failure compared to non-failure ones. Patients who went into respiratory failure showed a mean troponin T and CK-MB levels of 0.0895 ± 0.01 ng/ml and $34.65 \pm$ IU/L, respectively. The mean troponin T and CK-MB level in a patient who died were $0.1142 \pm$ ng/ml and $39.14 \pm$ IU/L, respectively.

Conclusion: OP compound can directly cause myocardial injury during the acute phase. Cardiac complications of OP poisoning can be life threatening and are not fully appreciated. The level of cardiac enzymes correlated well with the severity of poisoning and prognosis, suggesting its use as a prognostic indicator of OP poisoning. Vigilant monitoring of the patients for prominent cardiac manifestations such as QT prolongation, VT or VF, and prompt treatment can save many patients.

Key words: Bradycardia, Creatinine phosphokinase-MB, Electrocardiographic changes, Organophosphorus poisoning, Tachycardia, Troponin T

INTRODUCTION

Organophosphorus (OP) pesticide self-poisoning is estimated to kill around 200,000 people each year, largely in the Asia-Pacific region. This predominantly occurs in rural communities and is often an impulsive act comparable to self-poisoning with medication in the west; the critical difference being the 10–20% case fatality rate (compared to 0.3% in Britain for example).^[1] OP poisoning is also of

great interest to developed countries vulnerable to terrorist or military attack with nerve agents.^[1]

The principal pharmacological action of all OPs is the inhibition of acetylcholinesterase; most patients die from cardiorespiratory failure. However, there is much variation in the timing of onset and clinical features depending on the particular OP involved. OP poisoning has high inpatient mortality and many patients have cardiorespiratory arrests after admission (38% of patients requiring intubation in one study).^[2] Cardiac complications are common and can be fatal if not diagnosed and treated early. The exact pathogenesis of cardiac complications has not yet been defined. A few important studies have been carried out both in India and abroad to study the cardiac complications and

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electrocardiographic (ECG) changes in OP poisoning. The current study was carried out to understand the cardiac manifestations of OP poisoning with special reference to cardiac enzymes.^[3]

The cardiac manifestations occur in a majority of affected patients and may range from innocuous ECG 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 OP poisoning. The mechanisms of OP-induced cardiac toxicity are not fully understood. Aside from direct toxic effects of the OP compounds, an increase in sympathetic and/or parasympathetic activity, hypoxemia, acidosis, and electrolyte abnormalities are thought to be involved in myocardial damage associated with OP poisoning. The reported prevalence of various ECG changes in OP compound is 89.1%.^[3]

Both sympathetic and parasympathetic overactivities have been shown to cause myocardial damage.^[4] As early as 1974, Yasue *et al.*^[5] postulated that parasympathetic overactivity plays a major role in coronary artery spasm, and later, Horio *et al.*^[6] induced coronary artery spasm in adult humans with healthy coronary arteries after intracoronary injection of acetylcholine. In a series of 168 cases of OP poisoning reported by Kiss and Fazekas,^[7] five had a transient picture of myocardial infarction. Diffuse myocardial damage was found at necropsy in two cases of malathion poisoning (an old-generation OP).^[8]

The extent, frequency, and pathogenesis of the cardiac toxicity from OP compounds have not been clearly defined. A study conducted by Kathi *et al.*^[3] over a three year period of cardiac complication following organophosphate poisoning; 37 patients, 62.5% (23/37) developed cardiac complication, of which 29.7% (11/37) had ECG changes suggestive of myocardial damage (ST-T changes); the mortality rate was 8.1% (3/37).

CP Dalvi *et al.*^[9] studied the correlation of ECG changes in OP poisoning with its prognosis. Abnormal ST-T changes and progressive fall in voltage and/or low voltage were the most common ECG changes encountered. These occurred significantly more often in patients with moderate or severe poisoning ($P < 0.001$). The 17 patients (5 moderate and 12 severe) with a combination of these ECG abnormalities required higher doses of atropine (mean 30 mg), and in the 12 who survived, the ECG took longer (mean 5.5 days) to normalize (despite normal clinical recovery rate) as compared to other cases. All fatal cases in the study had both these ECG changes.

Jian-dong *et al.*^[10] studied the dynamic changes of cardiac enzymes and the acute poisoning with OP poisoning in the Department of Emergency, Sichuan Provincial People's Hospital. Fasting serum level of troponin T and cardiac enzymes (creatinine phosphokinase-MB [CK-MB], CK, aspartate aminotransferase, and lactic dehydrogenase) in 92 patients with acute OP poisoning (AOPP) were measured after poisoning 1, 2, 3, 5, and 7 days and were measured 1 time in normal control group as well. There was an increase of different levels in troponin T and cardiac enzymes along with the degree of AOPP. They concluded that the level of cardiac troponin T and cardiac enzymes in patients with AOPP may be as useful markers of degree of poisoning and prognosis.

Ya-ying *et al.*^[11] conducted a study at the People's Hospital of Yingshang, Anhui. They studied the applied value of serum cardiac troponin T (cTnT) for diagnosing myocardial lesion in the AOPP. The serum cTnT and CK-MB were significantly higher than that in control group and increased with the degree of poisoning. They concluded that the level of serum cTnT increases significantly with the serious degree of AOPP and was sensitive marker of myocardial injury.

Aims and Objectives

The aims of this study are as follows:

1. To study prevalence and predictors of outcomes of myocardial injury with troponin T and CK-MB as biomarkers in OP poisoning.
2. To correlate the myocardial injury with the clinical severity and outcome in OP poisoning.

MATERIALS AND METHODS

We prospectively studied a series of 50 patients admitted with a history of OP compound consumption. History was taken, general physical examination and a detailed systemic examination was done. Routine blood investigations were sent. Patients are classified into three grades using "Paradeniya OP poisoning scale." Changes in ECG were monitored, and serum CK-MB and troponin T levels were measured at admission and repeated after 3 days and at discharge. Troponin T levels ≥ 0.10 ng/ml and CK-MB levels ≥ 40 U/L were considered as statistically significant. The analysis of the data was done using appropriate statistical methods.

Method of Collection of Specimens and Processing

Inclusion criteria

All symptomatic patients having ingested OP compound with mild, moderate, and severe OP poisoning were included in the study.

Table 1: Distribution of patients according to their age group (n=50)

Bio-social characteristics	n (%)
Age (in years)	
<30	22 (44.0)
30–39	16 (32.0)
≥40	12 (24.0)
Mean±SD	33.06±13.41
Range	19–85

SD: Standard deviation

Table 2: Distribution of patients according to the clinical features

Clinical sign	n (%)
Tachycardia	15 (30.0)
Bradycardia	10 (20.0)
Hypertension	8 (16.0)
Hypotension	5 (10.0)

The most common clinical finding in patients was tachycardia (30%) followed by bradycardia (20%). Hypertension was seen in 8 (16%) patients and 5 (10%) showed hypotension

Table 3: Distribution of patients according to their ECG changes (n=50)

Characteristics	n (%)
ST elevation	16 (32.0)
Sinus tachycardia	15 (30.0)
QT prolongation	12 (24.0)
Sinus bradycardia	10 (20.0)

Most common ECG finding was ST elevation (32%), Sinus tachycardia (30%) and QT prolongation (24%). ECG: Electrocardiographic

Table 4: Distribution of patients according to their trop-T changes (n=50)

Trop-T positivity (>0.1 ng/ml)	n (%)
Day 1	0 (0.0)
Day 3	5 (10.0)
Discharge	0 (0.0)

Table 5: Distribution of patients according to their CK-MB changes (n=50)

CK-MB positivity (>40 U/L)	n (%)
Day 1	0 (0.0)
Day 3	5 (10.0)
Discharge	0 (0.0)

Markers of cardiac markers, troponin T and CK-MB were seen in 5 cases (10%). There was no evidence of raised enzymes in these 5 patients at admission or discharge. CK-MB: Creatinine phosphokinase-MB

Exclusion criteria

The following criteria were excluded from the study:

1. Patients who have ingested other substance in addition to OP.
2. Patients who are known to have pre-existing heart

disease such as rheumatic heart disease and ischemic heart disease.

3. Patients who are hypertensives.
4. Patients who are chronic alcoholics.
5. Patients with chronic kidney disease.

Statistical Analysis

Data were entered into Microsoft Excel and analyses were done using the Statistical Package for Social Sciences (SPSS) for Windows software (version 18.0; SPSS Inc, Chicago). Descriptive statistics such as mean and standard deviation for continuous variables and frequency and percentage for categorical variables were determined. The Chi-square test and Fisher's exact test (when appropriate) were used to show the associations between predictor and outcome variables. The level of significance was set at 0.05.

RESULTS

In this study which included 50 patients of OP poisoning, 66% were males and 34% were females. Majority of the patients were in the age group of <30 years, which constituted 44% of the study population. The severe poisoning group predominantly had an older population with a mean age group of 64 ± 15 years, when compared to mild (33.16 ± 10.84 years) and moderate (31.63 ± 10.17 years). Tachycardia seen in 30% of the patients was the most common finding, followed by bradycardia (20%), hypertension (16%), and hypotension (10%). ST elevation (34%) was the most common abnormality seen in ECG, followed by sinus tachycardia (30%), Q-T prolongation (24%), and bradycardia (20%). Q-T prolongation was associated with 47% of patients with respiratory failure and 71.42% of patients with death which was higher than patients without respiratory failure (3.7%) and survivors (16.27%). Positive cardiac enzymes were seen only in 10% of the patient, but all the patients in this group developed respiratory failure. The mean troponin T and CK-MB levels (0.1142 ± 0.06 ng/ml and 39.14 ± 8.23 U/L) were higher for patients who died when compared to the survivors. The similar picture was seen in patients who went into respiratory failure (troponin T 0.0895 ± 0.01 ng/ml and 34.65 ± 11.66 U/L) when compared to those without respiratory failure.

DISCUSSION

In this study, 50 patients of OP poisoning with cardiac manifestation of the poisoning were studied.

In this study, patient in the age group ranging from 19 years to 85 years were included with a mean age of 33.06 ± 13.41

Table 6: Association of markers of myocardial injury with respiratory failure (n=50)

Markers	No respiratory	Respiratory	P
	Failure (n=27)	Failure (n=23)	
CK-MB at day 3			
Positive	0	5	0.011
Negative	27	18	
Trop-T at day 3			
Positive	0	5	0.011
Negative	27	18	
ST elevation			
Present	9	7	0.827
Absent	18	16	
QT prolongation			
Present	1	11	<0.0001
Absent	26	12	

All 5 patients who had a positive CK-MB on 3rd day developed respiratory failure, 18 of 45 patients (40%) with CK-MB negative developed respiratory failure.
CK-MB: Creatinine phosphokinase-MB

Table 7: Association of markers of myocardial injury with mortality (n=50)

Markers	No mortality	Mortality	P
	(n=43)	(n=7)	
CK-MB at day 3			
Positive	4	1	0.684
Negative	39	6	
Trop-T at day 3			
Positive	4	1	0.684
Negative	39	6	
ST elevation			
Present	13	3	0.507
Absent	30	4	
QT prolongation			
Present	7	5	0.002
Absent	36	2	

CK-MB: Creatinine phosphokinase-MB

Table 8: Association of duration of ICU stay with mean Troponin T levels and CK-MB levels on day 3

Duration of ICU stay	Mean troponin T level	Mean CK-MB level
	(ng/ml) ± SD	(U/L) ± SD
<7 days	0.0438 ± 0.02	27.13 ± 9.68
>7 days	0.0957 ± 0.07	34.07 ± 10.51

SD: Standard deviation, CK-MB: Creatinine phosphokinase-MB

[Table 1]. Tachycardia (30%) was the most common clinical sign seen in the present study [Table 2]. Bradycardia which is an expected finding in OP poisoning was seen in 20% of the patients. Bradycardia was seen in all the 3 cases of severe poisoning, 6 of 22 (27%) cases of moderate poisoning, and 1 (4%) case of mild poisoning. Hence, bradycardia can be considered as an indicator of the severe degree of poisoning. Blood pressure changes in the form of hypertension (systolic blood pressure [BP] ≥140 and/or diastolic BP ≥90 mmHg) and hypotension (systolic BP ≤90 mmHg) were seen in 8 (16%) and 5 (10%) patients,

respectively. Three patients who developed hypotension did not recover and died after a prolonged intensive care unit (ICU) stay [Table 3].^[3]

In the current study, abnormal ECG was noted in 22 cases. The most common abnormality found was ST elevation (≥2 mm above the isoelectric line), which was found in 16 patients (32%), followed by sinus tachycardia in 15 patients (30%) and Q-T prolongation (Q-Tc ≥0.42 s in males and ≥0.43 s in females) in 12 patients (24%). Sinus bradycardia was found in 10 cases (20%) [Table 4].

Q-T interval prolongation was associated with 11 of 23 (47%) patients who developed respiratory failure and needed mechanical ventilator as compared to 1 of 26 patients (3.7%) without respiratory failure ($P < 0.0001$). Unlike Q-T interval, ST segment did not show any statistically significant relationship with the outcome ($P = 0.827$ for respiratory failure and $P = 0.507$ for mortality).

Markers of Myocardial Injury

In the present study, cardiac enzymes (troponin T and CK-MB) which are used as an indicator of cardiac injury were positive (troponin T ≥0.1 ng/ml and CK-MB ≥40 U/L) in 5 of 50 patients (10%) (mean value of 0.196 ± 0.03 ng/ml and 52.4 ± 6.84 U/L for troponin T and CK-MB, respectively) on the day 3 of admission [Tables 4 and 5]. All the patients who showed enzyme positivity also had ST-segment elevation on ECG, both of which reverted back at the time of discharge suggesting a transient ischemic process as described by Kiss and Fazekas.^[8]

All the 5 patients who showed raised cardiac enzymes developed respiratory failure, and 18 of 27 patients (66%) with normal cardiac enzymes developed respiratory failure ($P = 0.011$). Indicating that patients with raised cardiac enzymes have a higher chance of developing respiratory failure.

Cardiac enzymes were raised 1 of 25 (4%) patients in mild, 3 of 22 (13.6%) patients in moderate, and 1 of 3 (33.33%) patients in severe poisoning. Hence, raised cardiac enzymes were most commonly seen in severe poisoning; however, this relationship was not statistically significant ($P = 0.722$). Of the 5 patients who had raised cardiac enzymes, 1 died. This was also found not to have statistical significance ($P = 0.684$).

The mean troponin-T levels in mild, moderate, and severe group were 0.0412 ± 0.04 , 0.0833 ± 0.05 , and 0.0886 ± 0.01 ng/ml, respectively. Similarly, the CK-MB levels were 24.04 ± 7.86 , 36.40 ± 8.95 , and 38.88 ± 4.04 U/L in mild, moderate, and severe cases,

respectively. As can be seen, the troponin T and CK-MB showed increasing levels with increasing severity of poisoning. This trend was also seen in the study conducted by Jian-dong *et al.*^[9]

The mean troponin T and CK-MB value also showed a higher value in patients who died when compared to patients who survived. The mean value in a patient who died was 0.1142 ± 0.06 ng/ml and CK-MB was 39.14 ± 8.23 U/L which was higher than the levels seen in survivors (troponin T- 0.0565 ± 0.04 ng/ml and CK-MB 28.34 ± 10.056 U/L) [Table 6].

Thus, the higher troponin T and CK-MB values were associated with a higher incidence of mortality and respiratory failure, hence suggesting its use as a prognostic indicator [Table 7].

It was also seen that in patients who developed respiratory failure, higher titers of cardiac enzyme was associated with increased duration of ICU stay. In this study, the mean troponin T and CK-MB levels in patients with ICU stay <7 days were 0.0438 ± 0.02 ng/ml and 27.13 ± 9.68 U/L, and the mean troponin T and CK-MB levels in patients with ICU stay >7 days were 0.0957 ± 0.07 ng/ml and 34.07 ± 10.51 U/L, respectively [Table 8].^[12]

CONCLUSION

- The most common clinical sign related to cardiovascular system was tachycardia, as opposed to the expected finding of bradycardia, which was the second most common finding, but was associated with the severe degree of poisoning.
- Most common ECG finding was ST elevation, followed by Q-T prolongation. Prolonged QT interval was found to be indicator of severity and also had a

prognostic value in predicting death and respiratory failure.

- Cardiac enzymes when found positive was associated with higher likelihood of developing respiratory failure.
- The level of cardiac enzymes correlated well with the severity of poisoning, days of ICU stay and outcome, suggesting its use as a prognostic indicator of OP poisoning.

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