

A STUDY ON CARDIAC EFFECTS OF ACUTE ORGANO-PHOSPHORUS COMPOUND POISONING AND ITS POSTMORTEM TOXICOLOGICAL FINDINGS**¹Dr. V. N. Alaga Venkatesan, ^{2*}P. G. Anandhi, ³P. Shridharan and ⁴J. Durga Lakshmi**¹Associate Professor of General Medicine, Government Rajaji Hospital and Madurai Medical College, Toxicology incharge.²Associate Professor, Institute of Anatomy, Madurai Medical College.³Assistant Professor, Department of General Medicine, Government Rajaji Hospital and Madurai Medical College.⁴Post Graduate, Department of General Medicine, Government Rajaji Hospital and Madurai Medical College.***Corresponding Author: Dr. P. G. Anandhi**

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ABSTRACT

Context: Mortality and morbidity associated with organo-phosphorus compound poisoning are well known facts. Even though the most common complication recognized is respiratory failure, cardiac complications also occur after OP poisoning. The study is undertaken with an aim to assess the extent of the myocardial injury in OPC poisoning using clinical, ECG & biochemical parameters & to correlate them with the outcome of the event including the postmortem external toxicological findings of Heart. **Aims and objectives:** 1. To study the prevalence of OPC Poisoning in our hospital. 2. To study the prevalence of myocardial injury in OPC poisoning & to correlate it with in hospital mortality. 3. To study the postmortem findings of Heart in OPC Poisoning. **Settings and design:** Hospital based Prospective Observational study **Materials and methods:** The study was conducted on 50 patients who were admitted in Govt. Rajaji hospital, Madurai with history and features of OPC poisoning who fulfilled the inclusion & exclusion criteria. **Statistical Analysis:** Using statistical software, frequencies, range, mean, standard deviation and percentages were calculated. **Results:** In our study, out of 19 deaths noted, five died within 24 hours of consumption, 5 within three days and the rest died after 72 hours of consumption, which correlated directly with ECG changes, serum CK-MB and serum Troponin T levels. This observation indicates that the EARLY deaths are due to cardiac cause. **Conclusions:** Cardiac effects of acute Organo-phosphorus compounds should be anticipated during the first few days of exposure to prevent mortality in addition to respiratory failure.

KEYWORDS: Cardiac toxicity; CK-MB; Troponin T levels; OPC poisoning.**INTRODUCTION**

Even though the most common complication recognized is respiratory failure, cardiac complications may also occur after OP poisoning. Myocardial damage in OPC poisoning is multi-factorial and caused both by Sympathetic and Parasympathetic over-activity, the latter may cause coronary artery spasm.

The extent, frequency and pathogenesis of the cardiac toxicity from these compounds has not been clearly defined. Current knowledge is based only on limited studies & case reports.

MATERIALS AND METHODS**Study population:** Source of data:

The study was conducted on 50 patients with history of OPC poisoning who fulfill the inclusion & exclusion criteria getting admitted to Government Rajaji Hospital

& Madurai Medical College during the study period from April 2017 to September 2017.

Inclusion criteria

All patients with history of exposure to organophosphorus compound within previous 24 hours with characteristic clinical manifestations of OPC poisoning.

Exclusion criteria

- 1) Patients who have ingested other substances in addition to OPC.
- 2) Patients who are known to have pre-existing heart disease like Rheumatic heart disease, Ischemic heart disease etc.
- 3) Patients who are hypertensives.
- 4) Patients with chronic kidney disease, neuromuscular disorders.
- 5) Patients who are aged above 60 years.

Ethical Committee Approval: Obtained.

Study protocol

A previously designed proforma was used to collect the relevant demographic and clinical details of the patients. Patients were enrolled in the study after informed consent.

Patients were classified as per, Peradynia OPC poison scale to assess the severity at the time of presentation. Then Daily clinical monitoring with special emphasis on pulse rate, blood pressure, respiratory rate and ECG monitoring were done. Serial CK-MB measurements on Day 0, 3 and 7 were done. Serum Troponin-T measurement was done on day 3. Also Arterial blood gas analysis, serum electrolytes and serum cholinesterase measurement were also done and noted.

The course of illness, recovery and development of complications were noted along with appropriate treatment like adequate atropinisation, usage of Oximes and other supportive measures including initiation of mechanical ventilation. Thus the course of acute cardiac injury in OPC poisoning and its effect on the prognosis were observed. If the patient succumbs to illness the postmortem toxicological external appearances of the Heart were noted.

Statistical Analysis

The data collected in the study was formulated into a master chart in Microsoft office Excel and statistical analysis was done with the help of computer using statistical software package SPSS V.17 for windows. Using this software, frequencies, range, mean, standard deviation and percentages were calculated.

RESULTS

In our study, among 50 patients who consumed OPC, most of them were in the age group of 31- 40 years (30%). The consumption rate was high among males (64%) and majority of them were educated(64%). The

most common reason for intentional consumption was Familial stress(38%).

Tab 1: Depicting the severity status of the patients at the time of admission according to Peradynia OP Poisoning Scoring system.

Severity Status	No. (%)
Mild	12 (24.0)
Moderate	23 (46.0)
Severe	15 (30.0)
Total	50 (100.0)

Score: Mild(0 -3) Moderate (4-7) Severe (8 -11)

Analysis of agents consumed revealed Lice killer liquid to be the most potent cardio-toxic agent (4 out of 9 deaths) while, Kurunai powder was the most potent agent to cause respiratory failure (5 out of 10 deaths). But, Exact quantity consumed by these patients couldnot be assessed with accuracy.

In our study, out of 50 patients enrolled, totally 19 patients succumbed to death, of which 10 died due to respiratory failure and 9 died of cardiac cause. Of 31 survivors, tracheostomy was done in 7 patients, thus reflecting the profound mortality and morbidity associated with OPC poisoning.

Out of 19 deaths noted, five died within 24 hours of consumption, 5 within three days and the rest died after 72 hours of consumption. This observation indicates that the EARLY deaths are due to cardiac cause.

ECG Changes

In our study, the ECG changes seen were Sinus bradycardia, Sinus tachycardia, ST-T changes, QTc Prolongation, Arrythmias and AV blocks. Sinus bradycardia was the most common ECG change noted on the day of admission (day 0) seen in 44% patients and sinus tachycardia was most common on day 1 of admission. This was seen in 70.2% patients and was most probably due to atropinisation.

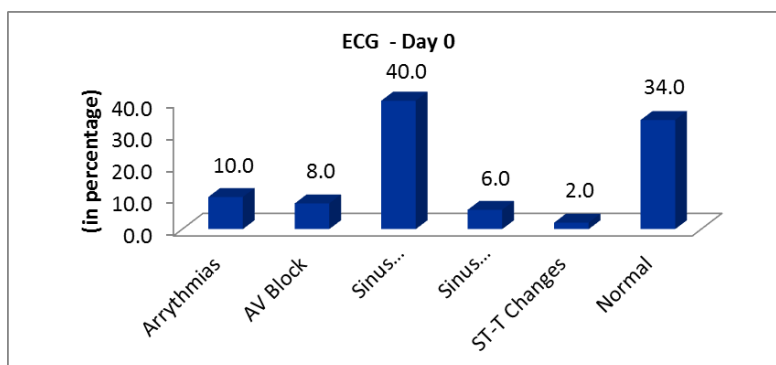


Fig 1: Depicting the ECG changes noted on Day 0 of consumption.

The presence of ARRHYTHMIA and AV BLOCK on day of admission and on day 1, 2 and 3, correlated well with mortality indicating significant cardiac effect of the compound consumed. QTc Prolongation was noted in 4

patients each on day 2 and day 3 of admission without progression to polymorphic VT of torsade de pointes type.

CK –MB Levels in OPC Poisoning

In our study, CK- MB levels elevation on day 0 and 3 of admission significantly correlated with mortality indicating the cardiac toxicity of the agent consumed.

The median values were 85 IU/L and 92 IU/L respectively. Day 7 Level of CK –MB was normal i.e., 18 IU/L which does not correlated with the death.

Table 2 & 3: Correlating the CK –MB levels on day 0 and day 3 of admission with cause of death.

	Cause of Death	
	Respiratory Failure (n=10)	Cardiac Cause (n=9)
	Median (IQR)	Median (IQR)
CK-MB Level – Day 0	19.0 (15, 21)	85.0 (79, 93)
P value	<0.001 (Significant)	

	Cause of Death	
	Respiratory Failure (n=8)	Cardiac Cause (n=3)
	Median (IQR)	Median (IQR)
CK-MB Level – Day 3	20.0 (16.7, 21.7)	92.0 (90.0, 92.0)
P value	0.014 (Significant)	

CK – MB levels on day of admission and on day 3 were found to be significantly elevated in patients who died of cardiac cause. This correlation was found to be statistically significant and the p value was <0.001 and p<0.014 respectively.

Troponin T Levels in OPC Poisoning

In our study, Troponin T levels done on day 3 were significantly elevated in three cases which correlated with their mortality. It was found to be normal in 8 patients who died of respiratory cause.

Table 4: Correlation of Day 3 Serum Troponin T levels with Cause of death.

	Reason for Death	
	Respiratory Failure (n=8)	Cardiac Cause (n=3)
	Median (IQR)	Median (IQR)
Trop T level	0.003 (0.003, 0.003)	0.020 (0.020, 0.030)
P value	0.010 (Significant)	

Elevation of Troponin T levels on day 3 were found to be statistically significant (p value 0.010) in three cases of death.

Out of 19 deaths noted, five died within 24 hours of consumption, 5 within three days and the rest died after 72 hours of consumption. This observation indicates that the EARLY deaths are due to cardiac cause.

External postmortem appearances of heart in deaths due to OPC poisoning

In our study, post mortem external appearances of heart revealed the following findings:

Heart appeared congested with petechial hemorrhagic spots. No clots were seen inside the cavities. Coronary arteries were completely patent. No visible areas of necrosis seen. Microscopic examination of myocardium was not done in our study.

DISCUSSION

Respiratory failure was considered to be the most common cause of death following OPC consumption according to many studies. However, Cardiovascular effects are quite common following acute OP poisoning, which are often more serious and fatal.

As per our study, OPC poisoning is the main suicidal agent, most often preferred by young, economically productive age group with case fatality rate of 20%.^[11]

Our study revealed, based on Peradynia scoring system, 24% had mild toxicity, while 46% and 30% of patients had moderate and severe toxicity respectively, at the time of admission. But, Prognosis could not be accurately predicted at the time of admission with this clinical scoring system because, few patients admitted with moderate toxicity died in later course of illness.

Cardiac effects of organo-phosphorus compounds

Myocardial damage in OPC poisoning is **multi-factorial** and caused both by Sympathetic and Parasympathetic over-activity,^[1] the latter may cause coronary artery spasm. Ludormirsky et al^[2] described **three phases of cardiac toxicity after OPC ingestion** namely, Phase (1) A brief period of increased sympathetic tone; phase (2) a prolonged period of parasympathetic activity and Phase (3) QTc prolongation leading to torsade de pointes(TdP) and VF.

The other possible contributing factors to myocardial damage includes hypoxemia; acidosis; electrolyte abnormalities; respiratory failure; over-atropinisation and

even direct toxic effect of these compounds on myocardium.

ECG Changes

In our study, the ECG changes seen were Sinus bradycardia, Sinus tachycardia, ST-T changes, QTc Prolongation, Arrhythmia and AV block. Morteza et al^[4] reported ECG changes in 49 patients. Similarly Rafigh Doost et al^[3] reported such changes in 33 patients.

Sinus Bradycardia and Tachycardia: In our study, sinus bradycardia was the most common ECG change noted on the day of admission (day 0) seen in 44% patients and sinus tachycardia was most common on day 1 of admission. This was seen in 70.2% patients and was most probably due to atropinisation. Similar findings were reported by Karki et al^[4] and Yurumez et al.^[5]

The presence of **ARRHYTHMIA and AV BLOCK** on day of admission and on day 1, 2 and 3, correlated well with mortality indicating significant cardiac effect of the compound consumed. The most common arrhythmia encountered was Ventricular tachycardia.

In our study, QTc Prolongation was noted in 4 patients each on day 2 and day 3 of admission without progression to polymorphic VT of torsade de pointes type. Vasanthi perumal et al^[6] and Karki et al^[4] and Kathi P et al reported such similar changes in their patients. Moreover, Chaung et al^[7] reported QTc prolongation in 67 patients among 170 and in their group, mortality rate, respiratory failure rate and frequency of VPC were significantly higher than those of patients without QTc prolongation. According to Bar-Meir et al^[8] Predisposing factors for QTc prolongation and development of TdP includes older ages, female gender, low left ventricular ejection fraction, Left ventricular hypertrophy and presence of electrolyte abnormalities like hypokalemia and hypomagnesemia.

CK –MB Levels in OPC Poisoning

In our study, CK- MB levels elevation on day 0 and 3 of admission significantly correlated with mortality indicating the cardiac toxicity of the agent consumed. The median values were 85 IU/L and 92 IU/L respectively.

In a study by Dayand et al^[9] mortality was 39.47% as against 4.76% with normal creatine kinase. Median Day 7 Level of CK –MB was normal i.e., 18 IU/L which does not correlated with the death.

Troponin T levels in OPC poisoning

In our study, Troponin T levels done on day 3 were significantly elevated in three cases which correlated with their mortality. It was found to be normal in 8 patients who died of respiratory cause. Similar results were observed in a study done by Abbas et al.^[10]

Thus, higher serum levels of cardiac markers serves as predictor of death in patients with OPC poisoning as emphasised by Davies et al.^[11]

Serum cholinesterase and OPC poisoning

In our study, the low serum cholinesterase levels correlated with complication and outcome but it could not differentiate the cardiac risk from other causes. The Median ChE levels noted were 410 IU/L and 432 IU/L among patients who died of Respiratory and cardiac cause.

Similar effects were seen by Noura et al.^[2,7] According to them, serum ChE levels do not correlate with severity always, since the base line values varies widely among individuals. Hence, a single value cannot assess the severity, but a fall in levels on serial follow up will help in determining the prognosis.

External postmortem appearances of heart in deaths due to OPC poisoning

In our study, post mortem external appearances of heart revealed the following findings:

Heart appeared congested with petechial hemorrhagic spots. No clots were seen inside the cavities. Coronary arteries were completely patent. No visible areas of necrosis seen.

These features were similar to the findings described by VV Pillai^[12] and Nandy A^[13]

Microscopic features of Toxic myocarditis documented in literature includes dilatation of pericardial blood vessels with hemorrhages in the surrounding tissues, interstitial edema of myocardium and presence of inflammatory cells. However, microscopic examination of myocardium was not done in our study.

CONCLUSION

The nature and quantity of agent consumed, severity of the poisoning, presence of other co-morbid illnesses, the stage at which treatment was initiated, adequacy of treatment, the presence or absence of intensive care facilities, early anticipation, identification and prompt treatment of complications are the main determinants of the In-patient outcome in case of OPC poisoning.

Deaths due to OPC poisoning can be classified as, EARLY and LATE deaths. Most of the EARLY deaths are due to cardiac effects which are potentially preventable and treatable if they are anticipated and recognized early. Hypoxemia, electrolyte disturbances and acidosis are the major predisposing factors for cardiac toxicity.

Assessment of cardiac toxicity can be done with serial ECG monitoring, Serial CK –MB and Trop T levels which directly correlates with the myocardial damage.

Hence, Cardiac effects of acute Organo-phosphorus compounds should be anticipated during the first few days of exposure to prevent mortality.

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