

Original Research Article

Troponins can it determine the outcome in acute organophosphorus poisoning?

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ABSTRACT

Background: India has shown a sharp rise in the number of suicidal poisoning in the past few years and organophosphorus compounds are the most commonly implicated. This is a prospective study done to assess if troponins can be used as a prognostic marker in patients with organophosphate poisoning.

Methods: Author conducted a prospective study on 50 patients to measure the level of troponin T and CK-MB on admission and Day 3 in patients with OP poisoning. This was then correlated to the severity of poisoning and also studied for its association with outcomes like respiratory failure or death. The primary endpoints were death and respiratory failure while secondary endpoint was the length of ICU stay.

Results: With 0.1 ng/ml taken as the cut off for Troponin- T, and 40 U/L for CK-MB, positive cardiac enzymes were seen only in 10% of the patients, 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. A similar picture was seen in patients with respiratory failure (Troponin T 0.0895 ± 0.01 ng/ml and 34.65 ± 11.66 U/L) as compared to those without respiratory failure.

Conclusions: The level of cardiac enzymes correlated well with the severity of poisoning, days of ICU stay and outcome, thus suggesting its use as a prognostic indicator of organophosphorus poisoning.

Keywords: CK-MB, Developing countries, Myocardial, Organophosphorus, Poisoning, Troponin

INTRODUCTION

Since the discovery of the specific subunit for troponin by Greaser et al, in 1973, troponin has been used widely as a marker for cardiac injury in a variety of medical conditions.¹ Troponin is organ specific and not disease specific, hence it acts as an indicator of myocardial stress.² As per previous research, organophosphorus poisoning has been shown to involve the heart, as indicated by the EKG changes and its positive association with mortality.³

Respiratory failure has been proven to be the most common cause of death in organophosphorus poisoning, either due to acute neuromuscular blockade or intermediate syndrome.⁴ But despite adequate ventilatory support, the mortality still seems to be high, especially in the low to mid income countries.⁵

Hence this study is an attempt to look into the Cardiac markers (troponin and CK-MB) as an indicator of myocardial injury in acute organophosphorus poisoning and to determine if involvement of the heart could be a

factor contributing to mortality and morbidity. This study is relevant especially for developing countries where a rising population has led to exponential agricultural growth, and with it, the increasing use of pesticides like organophosphorus compounds.⁶

METHODS

The type of study observational prospective non-randomized study was done. The Period of study with 50 adult patients for a period of 21 months (December 2011 to August 2013), who satisfied the inclusion and exclusion criteria (given below), admitted to a tertiary care hospital in India.

The methodology followed All the patients on arrival received adequate care as per the latest hospital and poisoning protocol. The purpose of the study was explained and informed consent obtained either from the patient or from the next of kin. Data was collected using a pre-tested proforma meeting the objectives of the study. Detailed history, physical examination and necessary investigations were undertaken. Patients were classified into three grades using ‘Paradeniya organophosphorus poisoning scale.’⁷. Changes in ECG were monitored and serum Creatinine phosphokinase–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 Creatinine kinase - MB levels ≥ 40 U/L were considered as significant. Troponin T levels were estimated by ELISA and Creatinine Phosphokinase MB were measured using IFCC method. All the patients were transferred to the ICU and closely monitored.

Statistical analysis

Data was 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 (SD) for continuous variables, and frequency and percentage for categorical variables were determined. The chi-square test and fisher’s exact test (when appropriate) was used to show the associations between predictor and outcome variables. The level of significance was set at 0.05.

Inclusion criteria

- All symptomatic patients having ingested organophosphorus compound with mild, moderate and severe organophosphorus poisoning.

Exclusion criteria

- Patients who have ingested other substance in addition to OP will also be excluded.
- Patients who are known to have pre-existing heart disease like Rheumatic Heart disease, Ischemic heart disease etc.

- Patients who are hypertensive.
- Patients who are chronic alcoholics.
- Patients with chronic kidney disease.
- Patients who are below the age of 12 years.

RESULTS

The study which was done on 50 patients showed that males (66%) predominantly constituted the study population, with only 34% being females. When the study population was segregated based on age, the majority (44%) was formed by a relatively younger population with age less than 30 years. Most of the patients presented with mild- moderate severity of poisoning as per Peradeniya organophosphorus poisoning scale.⁵ A very small group of patients presenting with severe level of poisoning. When 0.1 ng/ml was taken as the cut off for Troponin- T, and 40 U/L for CK-MB, 5 patients (10%) were considered to have significant elevation (positive value). Among the 50 patients, 7(14%) patients died, while 23 (46%) developed respiratory failure re-quiring intubation with mechanical ventilation (table 1). Majority of the patients required a short ICU stay (<7 days) with only a few requiring prolonged intubation (30%).

Table 1: Distribution of patients according to their outcome (N = 50).

Outcome	No. of patients	Percentage of patients
No respiratory failure	25	50.0
Respiratory failure	23	46.0
Death	7	14.0

Analysis

All 5(100%) patients who had a positive Troponin T and CK-MB, developed respiratory failure on Day 3, while 18 of 45 patients (40%) with negative Troponin T and CK-MB, developed respiratory failure on Day 3 (Table. 2). 1 of the 5 (20%) patients with positive Troponin T, died, as compared to 6 of the 45(13%) patients with negative Troponin T (Table. 3)

Table 2: Association of markers of myocardial injury with respiratory failure.

Outcome	No Respiratory Failure (n=27)	Respiratory Failure (n=23)	p value
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	

Table 3: Association of markers of myocardial injury with mortality (N = 50).

Outcome	No mortality (n=43)	Mortality (n=7)	p value
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	

Troponin T positivity was seen in 1 of 25 (4%) patients with mild, 4 of 22 (18.18%) with moderate and 1 of 3 (33.33%) patients with severe poisoning (Figure. 1)

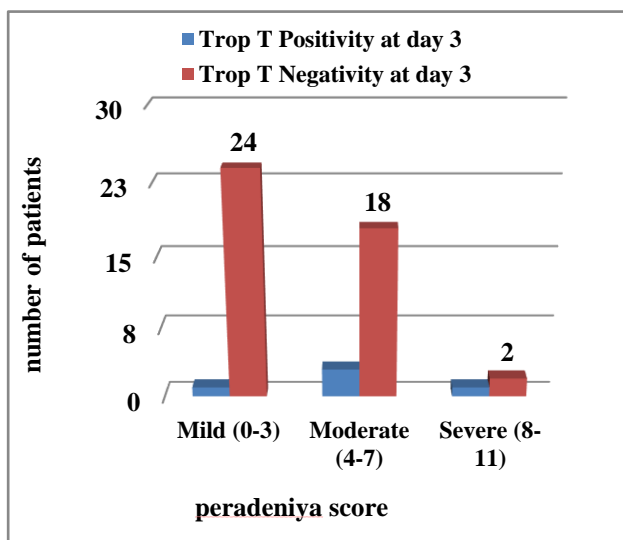


Figure 1: Association of clinical severity with Troponin T positivity (day 3).

With increasing severity of poisoning, a corresponding increase was noted in the Mean Troponin T and Mean CK-MB levels on Day 3 (Table 4). In other words, higher levels of Troponin T and CK-MB on Day 3 were associated with higher severity of poisoning.

Table 4: Association of clinical severity (peradeniya score) with mean troponin T levels and CK-MB levels on day 3.

Association of mean cardiac enzyme levels with clinical severity	Mean troponin T level (ng/ml) ±SD	Mean CK-MB level (U/L) ±SD
Mild (0-3)	0.0412±0.04	24.04±7.86
Moderate (4-7)	0.0833±0.05	36.40±8.95
Severe (8-11)	0.0886±0.01	36.66±4.04

The mean Troponin T and CK-MB level on Day 3 showed a higher value in patients who died, as compared to patients who survived, thus establishing a relationship

between level of Troponin T, CK-MB and mortality. (Table 5)

Table 5: Association of mortality with mean troponin T levels and CK-MB levels on day 3.

Association of Mean Level of cardiac enzymes with mortality	Mean Troponin T level (ng/ml) ±SD	Mean CK-MB level (U/L) ±SD
Mortality	0.1142±0.06	39.14±8.23
No mortality	0.0565±0.04	28.34±10.06

A similar association was noted between the levels of mean Troponin T and CK-MB level on Day 3 and respiratory failure. A higher level of Troponin T and CK-MB was seen in patients with respiratory failure as compared to those without respiratory failure. (Table 6).

Table 6: Association of respiratory failure with mean Troponin T levels and CK-MB levels on day 3.

Association of mean level of cardiac enzymes with respiratory failure	Mean Troponin T level (ng/ml) ±SD	Mean CK-MB level (U/L) ±SD
No respiratory failure	0.0428±0.06	25.96±7.31
Respiratory failure	0.0895±0.01	34.65±11.66

Similarly, in patients with respiratory failure requiring ICU admission, a higher level of Troponin T and CK-MB was noted in patients with ICU stay for >7 days as compared to those with <7 days, thus indicating a comparatively poor prognosis in patients with higher levels of cardiac enzymes (Table 7).

Table 7: Association of duration of ICU stay with mean Troponin T levels and CK-MB levels on day 3.

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

DISCUSSION

In the present study, cardiac enzymes (Troponin T and CK-MB) which were 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 (10%) patients (Mean value of 0.196±0.03 ng/ml and 52.4±6.84 U/L for Troponin T and CK-MB respectively) on day 3 of admission. This was similar to the study done by Saadeh et al, which also showed enzyme positivity in 10% of the cases.⁸ All the

patients who showed enzyme positivity also had ST segment elevation on ECG, both of which reverted back to normal levels at the time of discharge, thus suggesting a transient ischemic process as described by Kiss and Fazekas.⁹

All the 5(100%) patients who showed elevated cardiac enzymes, developed respiratory failure, while 18 of 27(66%) patients with normal cardiac enzymes developed respiratory failure (p value 0.011). This indicated that patients with elevated cardiac enzymes have higher chance of developing respiratory failure.

Cardiac enzymes were raised in 1 of 25(4%) patients with mild, 3 of 22(13.6%) patients with moderate and 1 of 3(33.33%) patients with severe poisoning. Hence, elevated levels of cardiac enzymes were most commonly seen in severe poisoning, however this relationship was not statistically significant (p value 0.722). Of the 5 patients who had elevated cardiac enzymes, 1 died. This was also not statistically significance (p value 0.684). This result might be attributable to the small sample size; hence a larger study population would be necessary to confirm the results.

There was no statistically significant association between positivity of cardiac enzymes and severity of poisoning. 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. Thus, it can be seen that Troponin T and CK-MB showed increasing levels with increasing severity of poisoning. This trend was also seen in the study conducted by wang jian-dong et al.¹⁰(Table 8 and 9)

Table 8: Comparison of troponin T levels changes with other studies.

Comparison of Troponin T level changes with other studies	Wang jian-dong et al, ¹⁰ (ng/ml)	Present study (ng/ml)
Mild	0.06±0.010	0.0412±0.04
Moderate	0.10±0.01	0.0833±0.05
Severe	0.16±0.02	0.0886±0.01

Table 9: Comparison of CK-MB levels changes with other studies.

Comparison of CK-MB level changes with other studies	Wang jian-dong et al, study 10 (U/L)	Present study (U/L)
Mild	37.1±5.6	24.04±7.86
Moderate	68.3±9.71	36.40±8.95
Severe	112.4±12.5	38.88±4.04

Similar to the association between severity of poisoning and cardiac enzymes, there was no statistically significant association between elevated cardiac enzymes and mortality. But, the mean Troponin T and CK-MB value showed a higher value in patients who died as compared to patients who survived. The mean value in 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).From this study it was noted that higher Troponin T and CK-MB values were associated with a higher incidence of mortality and respiratory failure, thus suggesting its use as a prognostic indicator.

It was also seen that in patients who developed respiratory failure, higher titres of cardiac enzymes were 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 was 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 was 0.0957±0.07 ng/ml and 34.07±10.51 U/L respectively.

CONCLUSION

There are factors other than respiratory failure due to neuromuscular blockade which can affect the morbidity and mortality. Through this study author have shown that myocardial injuries can be a contributing factor affecting the same. Hence a larger prospective study should be done to confirm the involvement of these cardiac markers in prognostication of acute organophosphorus poisoning patients.

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Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

- Greaser ML, Gergely J. Purification and properties of the components from troponin. J Biol Chem. 1973;248(6):2125-33.
- Park KC, Gaze DC, Collinson PO, Marber MS. Cardiac troponins: from myocardial infarction to chronic disease. Cardiovasc Res. 2017;113(14):1708-18.
- Balouch GH, Yousfani AH, Jaffery MH, Devrajani BR, Shah SZA, Baloch ZAQ. Electrocardiographic Manifestations of Acute Organophosphate Poisoning. World Applied Sci J. 2012;16(8):1118.
- Eddleston M, Aardema H, Meertens JH, Ligtenberg JJ, Peters-Polman OM, Tulleken JE. The pathophysiology of organophosphorus pesticide self-poisoning is not so simple. Neth J Med. 2008;66(4):146-8.
- Eddleston M, Phillips MR. Self poisoning with pesticides. BMJ. 2004;328(7430):42-4.

6. World Health Organization. WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification 2000-2001. Geneva; World Health Organization; 2001. Available at: https://www.who.int/ipcs/publications/pesticides_hazard_2009.pdf. Accessed 9 October 2013.
7. Senanayake N, De Silva HJ, Karalliedde L. A scale to assess severity in organophosphorus intoxication: POP scale. *Hum Experi Toxicolog.* 1993;12(4):297-9.
8. Saadeh AM, Farsakh NA, Al-Ali MK. Cardiac manifestations of acute carbamate and organophosphate poisoning. *Heart.* 1997;77(5):461-4.
9. Kiss Z, Fazekas T. Arrhythmias in organophosphate poisonings. *Acta Cardiologica.* 1979;34(5):323-30.
10. WANG J, CHEN Kang, XU Hui. The Change of Cardiac Enzymes and Troponin T in Patients with Acute Organophosphorus Pesticide Poisoning. *West China Med J.* 2007;4-052.

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