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# Creatine Phosphokinase N-Acetyl-Cysteine Level as a marker of severity in acute organophosphorus poisoning: A Prospective Study at medical college, Hospital Rajasthan

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## Abstract

**Background:** The objective of our study was to measure the Creatine Phosphokinase N-Acetyl-Cysteine Level in acute organophosphorus poisoning

**Methods:** This study was conducted among minimum 100 patients acute organophosphorus poisoning admitted in Casualty ward, MICU and attending medical ward of JLN hospital, Ajmer during Aug 2018 to July 2020. Creatine phosphokinase N-acetyl-cystein - Serum creatine phosphokinase N-acetyl-cysteine estimation by spectrophotometric analysis using Beckman Coalter AU 680.

**Results:** The mean values of CPK-NAC were found to be 524.11±352.848 on day 1 and 481.77±394.04 on day 3. The mean values of CPK-NAC were significantly higher among deaths on day 1 and 3(778.14±356.78 and 1045.45±423.75, respectively) in comparison to survivors on day 1 and 3 (452.46±318.93 and 322.78±185.11, respectively). Significant difference was found between mean values of different levels of severity of CPK-NAC on day 1 and 3.

**Conclusion:** Serum Creatine Phosphokinase N-Acetyl-Cysteine (CPK-NAC) are efficient biomarker in case of acute OP poisoning not only due to its easy availability and low cost, but also because serial monitoring of its level during the entire course of therapy can predict the prognosis.

**Keywords:** CPK-NAC, OP poisoning, Biomarker

## Introduction

Organophosphorus (OP) compound is one of the common causes of poisoning in rural India as they are easily available.[1] OP poisoning leads to three main syndromes: Acute cholinergic syndrome, intermediate syndrome (IMS), and OP induced delayed neuropathy (OPIDN).[2]

Various prognostic tools such as serum creatine phosphokinase N-acetyl-cysteine (CPK-NAC), lactate dehydrogenase (LDH), serum immunoglobulins, and circulating complements for early detection of patients at high risk for developing respiratory failure have been tried.[3] There will be the elevation of serum CPK in OP poisoning due to myonecrosis caused by persistent

depolarization at the neuromuscular junction and oxidative cellular damage to muscle membrane. Serum CPK – NAC level has also been studied as a predictor for the onset of IMS, but in earlier studies CPK has been measured only at admission and/or prior to discharge[4-6]

The objectives of our study were to measure serial serum CPK-NAC levels, correlate CPK-NAC levels with severity of poisoning.

**Material and Methods**

This study was conducted among minimum 100 patients acute organophosphorus poisoning admitted in Casualty ward, MICU and attending medical ward of JLN hospital, Ajmer during Aug 2018 to July 2020.

**Inclusion Criteria**

- On the basis of history of ingestion of organophosphorus compounds as said by the patient or attendant.
- On the basis of clinical signs and symptoms of OP poisoning.
- On the basis of improvement of signs and symptoms after treatment with atropine and oximes.
- On the basis of pseudo cholinesterase level (if needed).

**Exclusion criteria**

1. Patients with mixed poisoning; OP poisoning and any other poison like organocarbamate, organochlorous compound etc.
2. Chronic alcoholic patients.
3. Patients having diabetes mellitus and any renal disease.
4. Patients having h/o malignancy and auto immune disease.
5. Patients with co-existing illness myopathy, myocarditis, myocardial infarction, epilepsy.
6. Patients who had trauma or received intramuscular (I/M) injection and cardiopulmonary resuscitation recently or on prior medications like statins, fibrates and aspirin.
7. Patients who had hemolytic anemia and meningitis, encephalitis and other hemolytic conditions like sepsis.
8. Patients not include in inclusion criteria.

**Method of collection of data**

1. Informed consent was taken from eligible patients or legally authorized attendants. (If the patient was unconscious). Medico legal formality was done.
2. Qualifying patients was undergoing detailed history. Clinical examination, biochemical examinations.
3. After admission, through clinical examination was carried out and relevant investigations shall be performed.
4. All data was recorded as per the enclosed proforma within 48 hours.

**Peradeniya Organophosphorus (POP) Scale**

| Parameters | Findings | Scale |
|---|---|---|
| 1 Pupil size | >2mm | 0 |
| | <2mm | 1 |
| | Pinpoint | 2 |
| 2 Respiratory | <20/minute | 0 |

| | | |
|---|---|---|
| Rate | ≥20/minute | 1 |
| | ≥20/minute with cyanosis | 2 |
| 3 Heart rate | >60/minute | 0 |
| | 41-60/minute | 1 |
| | <40/minute | 2 |
| 4 Fasciculations | None | 0 |
| | Present ± generalized ± continue | 1 |
| | Both generalized and continue | 2 |
| 5 Consciousness | Conscious and oriented | 0 |
| Level | Impaired verbal response | 1 |
| | No verbal response | 2 |
| 6 Seizures | Absent | 0 |
| | Present | 1 |

0-3, Mild Poisoning

4-7, Moderate Poisoning

5-11, Severe Poisoning

**Sample Collection**

In all study subjects, 5 ml of plain blood was collected on admission before administration of atropine. Creatine phosphokinase N-acetyl-cystein - Serum creatine phosphokinase N-acetyl-cysteine estimation by spectrophotometric analysis using Beckman Coalter AU 680. The serum creatine phosphokinase N-acetyl-cystein normal range for a male is between 29-195 U/L while in female the serum creatine phosphokinase N-acetyl-cysteine normal range is between 29-170 U/L.

**Statistical Analysis**

All the parameters were tabulated. Mean, Standard deviation were analysed using SPSS 20 software. Chi-square test was the test of significance used for qualitative variables to find the association between them. T test was the test of significance used for comparing quantitative variables with qualitative variable. One-way Anova is used as test of significance to assess various parameters with the compound used for poisoning.

**Results**

Table 1: Demographic Data of the Studied Patients

| | Frequency | Percent |
|---|---|---|
| Age (Years) | | |
| <20 | 36 | 36.0 |
| 20-30 | 40 | 40.0 |
| 30-40 | 18 | 18.0 |
| >40 | 6 | 6.0 |

| | | |
|---|---|---|
| Gender | | |
| Female | 30 | 30 |
| Male | 70 | 70 |
| History | | |
| Accidental | 16 | 16.0 |
| Suicidal | 84 | 84.0 |
| Occupation | | |
| Farmer | 92 | 92.0 |
| Others | 8 | 8.0 |

It was found that maximum patients (76.00%) were of young age who were below 30 years of age. Among all admitted patients, 70.00% patients were male and 30.00% were female and 84.00% of all cases were suicidal cases. Regarding occupation, it was found that most of the studied patients were farmers (92.00%).

Table 2: Mean Values of CPK-NAC on Day 1 And 3

| | Minimum | Maximum | Mean | Std. Deviation |
|---|---|---|---|---|
| CPK-NAC day 1 | 167 | 1385 | 524.11 | 352.848 |
| CPK-NAC day 3 | 162 | 1602 | 481.77 | 394.040 |

The mean values of CPK-NAC were found to be 524.11±352.848 on day 1 and 481.77±394.04 on day 3.

Table 3: Mean Values of CPK-NAC among death and survivors on day 1 and 3

| | Death | Survivor | P value |
|---|---|---|---|
| Day 1 | 778.14±356.78 | 452.46±318.93 | 0.001 (S) |
| Day 3 | 1045.45±423.75 | 322.78±185.11 | |

The mean values of CPK-NAC among death and survivors on day 1 and day 3 were significantly different. These were significantly higher among deaths on day 1 and 3(778.14±356.78 and 1045.45±423.75, respectively) in comparison to survivors on day 1 and 3 (452.46±318.93 and 322.78±185.11, respectively).

Table 4: Correlation of CPK-NAC on Day 1 and 3 with Pop Score (Severity of Poisoning)

| CPK-NAC | POP Score | | | P value |
|---|---|---|---|---|
| | Mild | Moderate | Severe | |
| Day 1 | 391.2 ± 237.47 | 639 ± 372.71 | 673.65 ± 372.2 | 0.001 (S) |
| Day 3 | 283.38 ± 134.96 | 627.12 ± 479.39 | 737.63 ± 449.406 | 0.001 (S) |

Significant difference was found between mean values of different levels of severity of CPK-NAC on day 1 and 3. These were 391.2 ± 237.47, 639 ± 372.71 and 673.65 ± 372.2 on day 1 and 283.38 ± 134.96, 627.12 ± 479.39 and 737.63 ± 449.406 on day 3.

**Discussion**

In our study mean values of CPK-NAC were found to be 524.11±352.848 on day 1 and 481.77±394.04 on day 3. The mean values of CPK-NAC were significantly higher among deaths on day 1 and 3(778.14±356.78 and 1045.45±423.75, respectively) in comparison to survivors on day 1 and 3 (452.46±318.93 and 322.78±185.11, respectively). Significant difference was found between mean values of different levels of severity of CPK-NAC on day 1 and 3. These were 391.2 ± 237.47, 639 ± 372.71 and 673.65 ± 372.2 on day 1 and 283.38 ± 134.96, 627.12 ± 479.39 and 737.63 ± 449.406 on day 3.

Bhattacharyya et al. (2011)[7] reported that serum CK was elevated due to rabdomyolysis or intermediate syndrome which is an associated complication of OP poisoning.

John et al. (2003)[8] highlighted that muscle injury begins during the cholinergic crises and the severity of muscle injury is correlated to the severity of the cholinergic crises. The excess acetylcholine seen in OP poisoning leads to reversible myocyte injury and rise of different muscle enzymes, including CK.However,

Hassan et al. (2013)[9] reported that the main disadvantage of serum CPK-NAC as a biomarker for acute OP poisoning, its non-specificity. So, exclusion of other conditions and diseases that may cause its elevation in patients with acute OP poisoning is mandatory.

**Conclusion**

Serum Creatine Phosphokinase N-Acetyl-Cysteine (CPK-NAC) are efficient biomarker in case of acute OP poisoning not only due to its easy availability and low cost, but also because serial monitoring of its level during the entire course of therapy can predict the prognosis.

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