Role of Serum Amylase in Predicting Prognosis of Organophosphate Poisoning

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Abstract:

Background :

Organophosphates(OPs) are the most commonly used pesticides in the world. In an agrarian country like India, OPs are the most common cause of suicidal deaths due to pesticides. This observational study was conducted to assess the utility of estimation of serum amylase in the assessment of clinical outcomes in OP poisoning cases. The study aimed at finding an association between serum amylase and the severity of OP poisoning based on Peradeniya organophosphorus poisoning (POP) Scoring Scale and usefulness of serum amylase in assessing the prognosis in terms of ventilator requirement, duration of intensive care Unit (ICU) stay and mortality in OP Poisoning cases.

Materials and Methods: The study was conducted after institutional ethical clearance in hospitals associated with a tertiary health care center affiliated to a medical college in south India. 90 OP poison cases were recruited in this longitudinal study over a period of two years. Patients were clinically examined for a POP score; blood was analyzed for serum amylase levels on the first day of admission and patients were followed up till death or discharge from the hospital.

Results: 46.7% of the study population had elevated serum amylase levels. Serum

amylase showed a significant ($p<0.0001$)positive correlation with the severity of OP Poison based on POP Scoring System, increased duration of ICU Stay, ventilator requirement, and mortality.

Conclusion: Serum amylase an easily available laboratory investigation can be cost effective in the assessment of clinical outcomes in OP Poisoning and aid in the early prompt and vigorous management of OP Poisoning cases for a better outcome.

Keywords: clinical outcome in organophosphate poisoning, heart rate, intensive care unit stay, pupillary dilatation, respiratory rate, ventilator support

Introduction

The green revolution ushered in the increased use of pesticides. Organophosphates (OP) compounds are used across the world in agriculture and household gardens. In recent years, there is an increase in the incidence of suicidal and accidental poisoning cases due to the easy accessibility of OP compounds [1]. A recent World Health Organization (WHO) report estimates a fatality of more than 3 million annually worldwide as a result of various poisonings [2]. A research project conducted in South India reported 4% cases fatality in poisoning cases [3]. OP compounds are extensively consumption used for their application as herbicides, pesticides, and chemical conflict agents as nerve gases for example, Tabun, Sarin, etc. [4, 5].

According to WHO, fatalities due to poisoning count beyond 220,000 in developing countries like India. This figure could be just the tip of the iceberg as many cases of poisoning remain unreported, especially in third-world countries. In India, OP Compounds are among the commonly used poisons with suicidal intent [5, 6, 7]. OP compounds act by inhibiting enzymes acetylcholinesterase and butyryl cholinesterase which lead to hyper stimulation of cholinergic synapses. Clinical features and death in such cases occur, if untreated and are due to increased neuronal stimulation at different synapses within the body[8].

Peradeniya Organophosphorus Poisoning (POP) scoring scale is a grading method designed for assessing the severity of intoxication by OP compounds. Its usefulness has not been much worked over in the Indian scenario. POP scale introduced in 1993 is a simple and effective tool in determining the requirement for ventilator support to assist patient's breathing in OP poison cases [9]. Studies have reported significance of association of serum amylase values above the normal range done on the day of admission to the hospital to the development of respiratory failure. A study reported a significant correlation of serum amylase with severity and shock [10, 11]. The pathophysiology of elevation of amylase in OP compounds is due to the subclinical pancreatic damage caused by the OP compounds secondary to the parasympathetic overstimulation and hypersecretion of enzymes by the compounds, consistent with another study

done in India[11]. The hyperamylasemia due to pancreatic injury has been found to be predictive of subsequent respiratory failure [12]. Thus, serum amylase can be used as a tool in the assessment of clinical outcome in organophosphorus poisoning. Foreseeing clinical outcome and taking appropriate decisions regarding shifting patients to the intensive care unit (ICU), can help in further preventing death due to poisoning. This study aimed to find out the importance of serum amylase values in predicting the severity of OP poisoning with respect to requirement for mechanical ventilation, duration of ICU stay and mortality.

Materials and Methods

The study was started after getting approval and clearance from the institutional Ethics Committee (IEC KMC MLR 10-17/202). This longitudinal study was conducted on patients admitted to tertiary care hospitals in south Indian cities between October 2017 to September 2019. All the procedures followed were in accordance with the ethical standards. All the patients aged >18 years with a history of consumption or contact or inhalation of OP Poison (within 1 day of consumption or contact or inhalation and brought to hospital), including consumption of OP along with alcohol were included in this study. Patients with clinical features characteristic of OP Poisoning suggestive of muscarinic involvement (Salivation, Lacrimation, Urination, Defecation, Gastric cramps, Emesis - SLUDGE) were incorporated in our study. Patients/cases with a history of suspected chemical consumption more than two days' back were excluded from this study. So also those <18 years of age, suffering from chronic illnesses like chronic kidney disease, chronic cholecystitis, chronic alcoholics, pre-existing pancreatic disease (ultrasonography scan of the abdomen showing evidence of chronic calcific pancreatitis) or clinical signs of perforated peptic ulcer or ischemic bowel disease; cases in whom serum amylase values may be beforehand altered were excluded from this study.

Informed consent was taken from the patients and/or legally authorized representatives of the patients. Clinical particulars were taken in detail in accordance with self-structured proforma. History of/exposure to OP compounds in any manner as solutions, solid forms of powder or tablets or blocks, or gaseous form or application on the skin was enquired. Patients or aides of patients giving a history of consumption were requested to provide the container from which the compound was consumed to confirm the chemical. Patients were clinically examined. Serum amylase estimation was done for all the patients included in the study on day 1 of admission to the hospital. Gastric lavage samples were sent for toxicological studies. Peradeniya organophosphorus poisoning (POP) Scoring Scale was referred to evaluate the severity of OP Poisoning on the day of admission to the hospital. This scale consists of six parameters namely, pupil size, heart and respiratory rate, level of consciousness,

fasciculation, and seizures. Based on clinical features revealed for each parameter score is graded on a 3 point scale varying from 0-2, except for seizures it has two grades 0 which means absent and 1 for present. A total score of a maximum of 11(severe /critical condition) to a minimum of zero (mild) can be ascribed to the patient. Patients were followed and further classified based on those who required longer duration of stay in ICU, longer requirement of ventilator support for respiration, patients who were discharged and those who succumbed to intoxication.

Statistical analysis

The collected data was tabulated, coded and analyzed further using IBM SPSS [Statistical Package for the Social Sciences-version 22]. The results are presented as proportions and percentages, along with other summary measures. For comparison across the groups, Chi-square &Karl-Pearson's correlation tests were used. 'p' value of <0.05 was taken as statistically significant. Association between continuous variables was assessed using Student's t-test. To study the predictability of Serum Amylase levels a ROC Curve was plotted and the area under the curve was studied.

Results

A total of 90 organophosphorus patients were enrolled. Table 1 summarizes the socio–demographic details of study participants.

Table 1 Socio – Demographic Details of Study Participants.

Variables	Sub – groups	Frequency n(%)
Age in years	20 - 30	27(30)
	31 – 40	28(31.1)
	41 – 50	20(22.2)
	Above 50	15(16.7)
Gender	Males	61(67.8)
	Females	29(32.2)
Alcohol consumption	Yes	51(56.7)
	No	39(43.3)
POP score	Mild 0 to 3	43(47.8)
	Moderate 4 to 7	31(34.4)
	Severe 8 to 11	16(17.8)
Total		90(100)

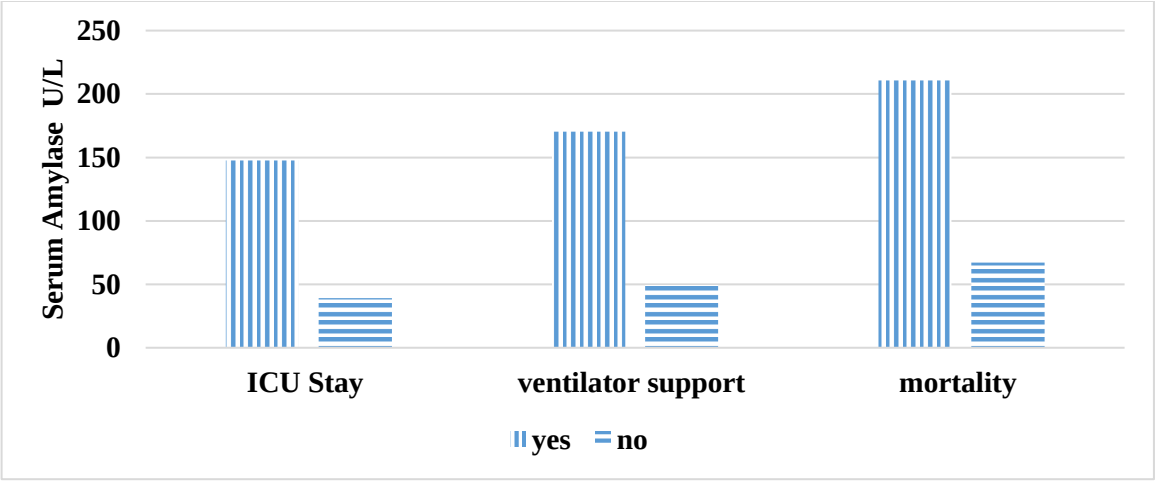
All patients studied were categorized for the severity of OP poisoning as per Peradeniya organophosphorus poisoning scale ranging from mild to severe. Mean serum amylase value was 46.93 U/L among patients with a mild POP score, while it was 125.42 U/L and 331.81 U/L among moderate and severe POP score patients. The correlation of rise in serum amylase values and presence of alcohol ingestion was not statistically significant (p value=0.733).

Table 2 Clinical Status of Participating Patients

Variables	Sub groups	N (%)
ICU stay	Yes	71 (78.9)
	No	19 (21.1)
Duration of ICU Stay(in days)	≤ 10	43(47.7)
	> 10	28(31.1)
Ventilator requirement during ICU stay	Yes	56(62.2)
	No	34(37.8)
Fatality / mortality	Yes	36(40)
	No	54(60)
Total		90(100)

Table 2 depicts clinical status of participating patients. 19 patients could be treated in wards without being admitted into ICU. Ventilator support was given to patients with respiratory failure. Serum amylase levels were measured in each sub - group of various categories. The mean serum amylase value was 147.52 U/L in patients who required hospital stay while it was 39 U/L in the other group. Similarly, serum amylase mean values were high in those who were given ventilator support being 170.29 U/L and 49.38 U/L in the non-ventilator group. 210.75 U/L was the average serum amylase value among the patients who succumbed to the poison, and 67.19 U/L in the survival group. Patients with high amylase levels had a longer ICU stay of more than 10 days.

Figure 1 Serum Amylase values and clinical Status of patient



p<0.0001

Discussion

In the present world, OP compounds are used extensively in household gardens and agricultural fields. This easy availability has increased the tendency of usage of these chemicals for poisoning, be suicidal, homicidal or accidental, especially in agrarian and developing countries. The toxic

effects of OP compounds are mainly due to the inhibition of enzyme acetyl cholinesterase in the nervous system leading to the accumulation of excess of acetylcholine at the synapses and myo-neural junctions. The clinical profile of patients who consumed OP Compounds depends upon the nature of the organophosphorus compound and whether inhibition of acetylcholinesterase is reversible or irreversible.

POP Scoring system developed in 1993, itis a simple and effective tool in determining the necessity for ventilator support while treating OP poison cases [9]. POP scoring has an advantage for use in unconscious patients as well as patients who are not cooperative or severely ill and are admitted in ICU. The parameters used in POP Scoring scale are representative of the muscarinic, nicotinic and central effects of the acute cholinergic phase. The score is obtained at the initial presentation, before any medical intervention.

Among the total 90 patients studied, (table 1)48% belonged to mild grade of poisoning based on POP score, 34% belonged to moderate grade and only 18% of patients had severe grade scoring. Correlation between severity of poisoning and serum amylase as per POP Scoring Scale was statistically significant ($p < 0.0001$). The pathophysiology of elevation in amylase level with OP Compounds can be related to the subclinical pancreatic damage caused by the OP Poison. This finding was consistent with another study which showed, organophosphates caused an increase in intraductal pressure and excessive pancreatic flow rate that results in extravasation of fluids, nevertheless pancreatic damage was mild and transient [12].

Another research work reported transient elevation of amylase in 52 of 100 patients with OP poisoning[13]. Acute pancreatitis is uncommon following acute anticholinesterase poisoning, although mild elevations of serum amylase are commonly seen after OP Poison consumption. In a recent study, reported 44% OP poison cases had elevated amylase levels and quoted increased gastrointestinal secretion as a probable cause for same [14]. The majority of the patients in our study had consumed OP Poison (84%) with a suicidal intention as per history provided during investigation. Since OP compounds are readily available as pesticides and open access to these compounds at pesticide shops may be the reason for OP compounds to be used as a common mode of suicidal attempt. Similar other study, observed comparable values [14, 15].

Respiratory failure requiring ventilator support was observed in 62.2% of patients in our study. Hyperamylasemia i.e serum amylase>96 U/L was observed in 46.7% of the patients. The correlation of amylase with the severity of OP Poison based on Ventilator support was found to be statistically significant ($p < 0.0001$). This was consistent with other parallel studies, which reported that the elevation of amylase was high in respiratory failure [16]. Hence,

amylase could be used as a predictor for early intubation and requirement of mechanical ventilation.

In our study, 71 patients were admitted in the ICU and the remaining were treated in the wards. It showed a significant correlation with the elevated amylase levels and the duration of ICU Stay ($p < 0.0001$). Patients with high amylase levels stayed for more than 10 days in the ICU and most of them required ventilator support.

In our study 34 patients expired out of the 90 patients (40%). There were many reasons attributable to the mortality namely the OP Poison itself, respiratory failure associated with the OP Poison, neurological causes such as seizures, coma. Cardiac causes like arrhythmia, sudden cardiac death, etc. also contributed to the mortality, in 40% cases of our study group. There was a significant correlation between the elevation of serum amylase and the mortality associated with poisoning ($p < 0.0001$).

Conclusion

46.7% of the study population had elevated serum amylase levels. Elevated amylase levels statistically correlated well with the severity of OP Poisoning based on POP Score. Elevated amylase levels had a significant association with the prolonged ICU stay, presence of respiratory failure, need for ventilator support and incidence of mortality. Thus, elevated serum amylase enzyme levels have a strong positive correlation with the severity of organophosphorus poisoning measured on the day of admission to the hospital. Estimation of serum amylase is an easily available laboratory investigation and cost-effective. It can be used as a tool in the assessment of clinical outcomes in OP Poisoning, help in taking early decision towards vigorous treatment and interventions of OP poison patients, thus, assisting in the prognostication and management of OP Poisoning in a much better manner.

Conflict of interest: Nil

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