ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 08, 2023

Original article

Acute pancreatitis as a prognostic marker in acute organophosphate poisoning

Dr Sandeep Prakash Kher*

*Associate Professor, Department of General Medicine, Ram Krishna Medical College Hospital and Research Center, Bhopal, Madhya Pradesh

***Corresponding Author: Dr Sandeep Prakash Kher**, Department of General Medicine, Ram Krishna Medical College Hospital and Research Center, Bhopal, Madhya Pradesh

Mob no: 9867300386

Email address: drsandeepkher@gmail.com

Conflict of Interest: none

Source of Support: Nil

Abstract

Background and Aim: Organophosphate (OP) insecticides are important compounds as the most probable common cause of acute poisonings in developing countries. OP intoxication often presents as medical emergencies, and its related morbidity and mortality have not decreased despite major advances in critical care. The present study was conducted to find the incidence of increased levels of serum amylase and serum lipase in OPC poisoning and to identify the relation with prognosis and clinical outcome, out of which one outcome was acute pancreatitis.

Material and Methods: The study was conducted at department of General Medicine, Tertiary care institute of Gujarat among the patients suffering from acute Organophosphate poisoning and admitted in emergency/ICU/medicine ward within 24 hours of intoxication event. This was an observational study conducted for the duration of 2 year with sample size of 85 patients out of which only 60 patients fulfill the inclusion and exclusion criteria. Patients were divided in 3 groups as mild, moderate and severe using q SOFA score at the time of admission.

Results: Mean serum amylase level values in various q SOFA categories (0, 1, 2 and 3) were 65.03, 81.95, 118.8 and 330.78 IU/l respectively with p value < 0.001 and that of mean serum lipase level values were 41.45, 44.2, 38.9 and 115.69 IU/l respectively with p value 0.05. Serum amylase levels were positively correlated with duration of ICU stay and were better predictor for acute pancreatitis.

Conclusion: Organophosphate poisoning is associated with multiple complications, including acute pancreatitis. The study found that levels of serum amylase & lipase were increased in statistically significant number of cases of acute organophosphate poisoning.

Key Words: Acute pancreatitis, Organophosphate poisoning, Serum amylase, Serum lipase

Introduction

Acute organophosphate poisoning is one of the commonest poisoning and has reached epidemic proportions in most parts of the world especially in developing countries where its management is lacking leading to high fatality rate. According to WHO, worldwide estimate of pesticide poisoning is around 3 million each year, with around 2 million hospitalized from suicide attempt majority of which are actually intentional as it is readily available in every

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 08, 2023

home.[1,2] Suicidal attempt with these easily accessible agents is a major problem in developing countries.[3] These agents are also used in chemical warfare as nerve agents.[4] OP is absorbed rapidly via the oral, respiratory, or transdermal routes, and has a high level of morbidity and mortality, especially in developing countries.[5,6] The mortality rate of self-poisoning in developing countries is 10–20%, mainly caused by respiratory insufficiency secondary to central depression of respiration, muscle weakness, and/or direct lung effects by bronchospasm and bronchorrhea.[7,8] Because of high mortality risk, both the acute cholinergic crises and the intermediate syndrome are best managed in an intensive care unit, unless the poisoning has been very mild.

Most of these deaths occur in rural areas, where easy access to highly toxic pesticides turns many impulsive acts of self-poisoning into suicide.[9] In India OPC intake is the commonest method of suicide (40.5%) after hanging (49%). Hospital-based data suggest that barbiturates and copper sulfate were the commonly used agents for suicide in the years, 1972-1977; however, later they were replaced by OP compounds and aluminium phosphide. Organophosphate insecticides are responsible for as much as 75% of all poisonings in our country today. [10]

Several syndromes are associated with OP poisonings, like acute cholinergic crises, intermediate syndrome (IMS) which can proceed from ~20% of first, and OP-induced delayed neuropathy.[11] Both in experimental studies and in humans exposed to these compounds pancreatic damage had been reported. Pancreatic injury in humans may be painless and marked by elevated serum amylase, elevated serum lipase, hyperglycemia and glycosuria.[11] occasionally, symptomatic acute pancreatitis can occur. The incidence of the latter varies from 7–22% depending on type of study, compound characteristics and level of work up and investigations done.[12] The OP compounds act by inhibiting acetylcholine esterase enzyme at nerve endings and neuromuscular junction, causing overstimulation of acetylcholine receptors. Signs and symptoms of poisoning are mainly due to muscarinic, nicotinic and central nervous system (CNS) receptor overstimulation.[13] The muscarinic receptor stimulation in pancreas yields increase in serum amylase and lipase levels. In acute OP poisoning, the severity of poisoning correlates with increase in serum amylase levels.[14]

Various scoring systems such as acute physiology and chronic health evaluation score (APACHE 2) are available, but laboratory evaluation plays an important and vital role for confirmation of poisoning, diagnosing the first acute organ damage and assessing the severity of poisoning.[15] In laboratory evaluation of OP poisoning, assessment of plasma cholinesterase is most specific lab test for OP poisoning, but serum amylase levels comes out to be the most sensitive lab test for OP poisoning. Increase levels of amylase and lipase are well documented in various studies and may be due to excessive cholinergic stimulation of pancreas.[16] The present study was conducted to find the incidence of increased levels of serum amylase and serum lipase in OPC poisoning and to identify the relation with prognosis and clinical outcome, out of which one outcome was acute pancreatitis.

Material and Methods

The study was conducted at department of General Medicine, Tertiary care institute of Gujarat among the patients suffering from acute Organophosphate poisoning and admitted in emergency/ICU/medicine ward within 24 hours of intoxication event. This was an

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 08, 2023

observational study conducted for the duration of 2 year with sample size of 85 patients out of which only 60 patients fulfill the inclusion and exclusion criteria. Patients of age >18 years of age (male and female) with acute (within 24 hours) organophosphate poisoning were included in this study.

Those patients with history of alcohol addiction or history of gall stones/gastric ulcer in the past were excluded. Patients with history of drug intake like azathioprine, valproic acid etc. were excluded.

Patient with history of acute OP poisoning (intake within last 24 hours) was admitted & selected for study as per inclusion and exclusion criteria. Using the qSOFA score, selected patients were divided into 3 groups (mild/moderate/severe). In all 3 groups (mild/moderate/severe), s. amylase and lipase levels were measured. In all 3 groups (mild/moderate /severe), Outcome variables like duration of ICU stay, need of intubation and radiological outcome variables like pancreatic size and echogenicity on ultrasound whole abdomen and relevant data is collected for statistical analysis.

Statistical analysis

The recorded data was compiled and entered in a spreadsheet computer program (Microsoft Excel 2007) and then exported to data editor page of SPSS version 15 (SPSS Inc., Chicago, Illinois, USA). For all tests, confidence level and level of significance were set at 95% and 5% respectively.

Results

Acute organophosphate poisoning was more prevalent among 18-42 years of age group with prevalence in females (63.3%) and males (36.6%). (Table 1) The serum amylase and lipase levels were distributed among all the cases in this study with non-normal distribution in positively skewed manner with few outliers (Table 2). Mean serum amylase level values in various q SOFA categories (0, 1, 2 and 3) were 65.03, 81.95, 118.8 and 330.78 IU/l respectively with p value < 0.001 (Table 3) and that of mean serum lipase level values were 41.45, 44.2, 38.9 and 115.69 IU/l respectively with p value 0.05 (Table 4).

Results of serum amylase levels were analyzed using one way ANOVA test or Welch test and it was found that higher serum amylase values were seen with higher values of q SOFA score which was statistically significant. ($p \leq 0.05$)

Results of serum lipase levels using Welch test were not significant. ($p > 0.05$) Following ROC curve is representative of accuracy of serum amylase levels in prediction of acute pancreatitis in patients with acute OP poisoning with sensitivity 98% and specificity 45% with Area under the curve (AUC) 0.97, which was statistically significant. ($p \leq 0.05$) In our study, 6.8% patients developed acute pancreatitis and showed edematous pancreas on ultrasound whole abdomen. Overall mortality was 17% in our study while 83% of recruited patients survived. Among the individual clinical severity group, mortality in mild group was 5.6%, in moderate group was 20% and in severe group was 31%. Estimates in represents log of odds of acute pancreatitis (bulky pancreas/normal pancreas).

Table 1: Gender wise Distribution of study Population

Gender	Number	Percentage (%)
Male	22	36.6
Female	38	63.3

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 08, 2023

Total	60	100

Table 2: Descriptive statistics of study populations

Variable	Serum amylase	Serum lipase
N	60	60
Mean	197	74.5
Standard deviation	97.45	48.64

Table 3: Frequency table of serum amylase level in relation to q SOFA category (welch test)

q SOFA	N	Mean s. amylase	SD
0	7	65.03	10.1
1	18	81.95	20.9
2	8	118.8	52.8
3	27	330.78	340.6

Table 4: Frequency table of serum amylase level in relation to q SOFA category (welch test)

q SOFA	N	Mean s. amylase	SD
0	7	41.45	6.2
1	18	44.2	11.03
2	8	38.9	10.64
3	27	115.69	135.22

Discussion

Multiple Cases of acute pancreatitis as a complication with organophosphate poisoning have been reported in literature.[17] Studies have been conducted in past to assess prognostic role of serum amylase and lipase levels in acute organophosphate poisoning and their relation with prognostic clinical scores like q SOFA score and APACHE 2 score.[18] Hyperamylasemia is frequent in severe OP poisoning and some authors considered it as a marker of OP poisoning.[19-21] Acute pancreatitis in adults with OP poisoning is estimated to be 12%, but hyperamylasemia because of low sensitivity and specificity is not a valid parameter in the diagnosis of OP-induced pancreatitis.[20,21] So, serum lipase may be useful for the early diagnosis of pancreatitis.[19] Tachycardia, as a most common clinical manifestation and associated with increased amylase, is a less frequent nicotinic sign, but here seems to arise mainly from atropine administration. The amount of received atropine is based on the continued stability of muscarinic signs and symptoms. Tachycardia, which is a symptom of atropinization, confirms adequate atropine intake. Therefore, it can be claimed that the severity and duration of muscarinic manifestation are related to prognosis. After justifying tachycardia, gastrointestinal symptoms are the most frequent presentation.

In our study, statistically significant increases in serum amylase and lipase level values were seen in patients with higher q SOFA score values. A positive correlation was also seen between serum amylase values and outcome variable with p value 0.041, however,

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 08, 2023

correlation between serum lipase values & duration of ICU stay was not significant, as per linear regression analysis. The positive correlation of serum amylase levels with poor clinical profile in our study was in accordance with the previous study like, in which the amylase levels were significantly elevated at the time of admission and had shown a gradual remission with proper treatment.[6] The mean amylase level in severely poisoned patients in their study was 295.02 U/l, while the mean amylase level in our study in severely poisoned patients was 330.78 IU/l. Serum amylase levels may be considered as a marker of Organophosphorous intoxication, since it enables the early recognition of severity and to identify those at risk of developing the complications of Organophosphorous poisoning. Acute pancreatitis as a complication of OP intoxication is not a rare condition and significant number of patients developed this complication. In order to improve the outcome of OP poisoning, early diagnosis of acute pancreatitis is important and serum levels of amylase and lipase should be routinely considered carefully. Hyperamylasemia and associated clinical severity found in our study was in accordance with the previous studies in which they carried out a retrospective study of medical records of 121 patients with the diagnosis of OP poisoning over three years in Veterans General Hospital, National Yang-Ming University in 1998.[22,23]

Oral ingestion of OP pesticides in a suicidal attempt is a major health problem especially in developing countries.[24] Diagnosis and aggressive management of acute poisoning with these lethal substances are required for decreasing morbidity and mortality.[25,26] Time of antidote administration seems to be a key factor in patient´s outcome.[27] Life-threatening intoxication is characterized by altered consciousness, seizure, urinary incontinence, and respiratory suppression. Respiratory failure is a most common complication and cause of death.

It was observed that 45 patients had hyperamylasemia. Lipase was measured in 30 patients with hyperamylasemia; ten of 30 had hyperlipasemia. In our study also, mean serum amylase levels in patients with qSOFA score=3 is 330.78 IU/l and mean serum amylase levels in patients of OP poisoning with ventilatory support was 354 IU/l. The finding of hyperamylasemia was closely related to clinical severity and presence of shock. Hence, it was concluded that hyperamylasemia is frequent in severe OP poisoning. However, hyperamylasemia is not synonymous with acute pancreatitis and pancreatic amylase is not reliable parameter in the diagnosis of organophosphate induced pancreatitis due to its low sensitivity, as it is also seen in our study that sensitivity of serum amylase levels in predicting clinical severity is around 65%. Our study was well correlated with the previous studies in which they studied that serum amylase, lipase and CPK were negatively correlated with plasma cholinesterase levels.[11,12] Serum amylase showed statistically significant negative correlation with plasma cholinesterase. Serum amylase showed the highest diagnostic accuracy for assessing severity of poisoning followed by CPK and Lipase. S Singh et al carried out a prospective study in PGI Chandigarh between 2001-2005 to find the incidence of acute pancreatitis with elevated levels of amylase and lipase in patients with organophosphate poisoning. Of the 79 patients studied, serum amylase was found to be elevated in 37 patients. It has been concluded that mild elevation of serum amylase is common in patients with organophosphate poisoning, however acute pancreatitis is rare but not uncommon.[28-30] There are also various studies which are well correlated with our study in one or other prospective.

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 08, 2023

Limitation of the study

Sample size was relatively small because all the patients of acute organophosphate poisoning do not meet the inclusion and exclusion criteria.

Conclusion

Organophosphate poisoning is associated with multiple complications, including acute pancreatitis. The study found that levels of serum amylase & lipase were increased in statistically significant number of cases of acute organophosphate poisoning. These levels can be used as prognostic marker in cases of acute organophosphate poisoning as well as levels of amylase & lipase were well correlated with the severity of acute organophosphate poisoning, which was assessed clinically, on admission using q SOFA score. We can say that serum amylase levels were well correlated with ultrasonographic pancreatic size, and can be used to measure prevalence of acute pancreatitis, an important complication of acute organophosphate poisoning which also affects mortality of these patients.

References

1. Brit C, Brahe BU, Cabecades M, Chisti P; Suicide Mortality in European Union. Eur J Pub Heal 2003; 13:108-114.

2. Farooqui AN, Tariq S, Asad F, Tariq O; Epidemiological profile of suicidal poisoning at Abbasi Shaheed Hosp Kar Med Dent Coll 2004;9:502.

3. Georgiadis G, Mavridis C, Belantis C, Zisis IE, Skamagkas I, Fragkiadoulaki I, et al. Nephrotoxicity issues of organophosphates. Toxicology. 2018; 406:129-36.

4. Rao AN, Patil A, Brodnik ZD, Liang Qiang, Rodrigo A España, Kimberly A Sullivan, et al. Pharmacologically increasing microtubule acetylation corrects stress-exacerbated effects of organophosphates on neurons. Traffic. 2017 Jul;18(7):433-441.

5. Davies JO, Eddleston M, Buckley NA. Predicting outcome in acute organophosphorus poisoning with a poison severity score or the Glasgow coma scale. QJM. 2008 May;101(5):371-9.

6. Jokanović M. Neurotoxic effects of organophosphorus pesticides and possible association with neurodegenerative diseases in man: A review. Toxicology. 2018 Dec 1;410:125-131.

7. Lorke DE, Petroianu GA. Reversible cholinesterase inhibitors as pretreatment for exposure to organophosphates. A review. J Appl Toxicol. 2019 Jan;39(1):101-16.

8. Eddleston M, Mohamed F, Davies JO, Eyer P, Worek F, Sheriff MH, et al. Respiratory failure in acute organophosphorus pesticide self-poisoning. QJM. 2006 Aug;99(8):513-22.

9. Wui-Chiang L, Chen-Chang Y, Jou-Fang D, MingLing W, Jiin G, Han-Chieh L, et al. The clinical significance of hyperamylasemia in organophosphate poisoning. Clin Toxicol. 2018;36(7):673-81.

10. Matsumiya N, Tanaka M, Iwai M, Kondo T, Takahashi S, Sato S. Elevated amylase is related to the development of respiratory failure in organophosphate poisoning. Hum Exp Toxicol. 1996;15(3):250-3.

11. Rohit N. Salame, Amar S. Wani, Study of serum amylase levels in organophosphate poisoning. Int J Biomed Adv Res. 2019;5:2229-3809.

12. . Sahin I, Onbasi K, Sahin H, Karakaya C, Ustun Y, Noyan T. The prevalence of pancreatitis in organophosphate poisonings. Hum Exp Toxicol. 2002; 21(4):175-7.

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 08, 2023

13. Poduval S, Patil RS, Vijayalaxmi RD, Patil V. Serum amylase levels in Organophosphorus poisoning and its prognostic significance A hospital based cross sectional study. J Int Med sRes Rev Rep. 2019;7(2):9- 14.
14. Sumathi ME, Kumar SH, Shashidhar KN, Takkalaki N. Prognostic significance of various biochemical parameters in acute organophosphorus poisoning. Toxicol Int. 2014;21(2):167-71.
15. Zobeiri M. Serum amylase as a prognostic marker of organophosphate poisoning. J Inj Violence Res. 2021; 13(2):117-120.
16. Sumathi ME, Kumar SH, Shashidhar KN, Takkalaki N. Prognostic significance of various biochemical parameters in acute organophosphorus poisoning. Toxicol Int. 2014;21(2):167-71.
17. Greenberger NJ, Toskas PP, Isselbacher KJ; Acute and chronic pancreatitis. In Fauci SA, Braunwald E, Isselbacher KJ, , et al.; eds. Harrison's principles of internal medicine, 14th edition. New York: McGraw-Hill, 1998:1741-52.
18. Peter JV, Thomas L, Graham PL, Moran JL, Abhilash KPP, Jasmine S, et al. Performance of clinical scoring systems in acute organophosphate poisoning. Clin Toxicol. 2013;51(9):850-4.
19. Hsiao CT, Yang CC, Deng JF, Bullard MJ, Liaw SJ. Acute pancreatitis following organophosphate intoxication. J Toxicol Clin Toxicol. 1996;34(3):343-7.
20. Lee WC, Yang CC, Deng JF, Wu ML, Ger J, Lin HC, etal. The clinical significance of hyperamylasemia in organophosphate poisoning. J Toxicol Clin Toxicol. 1998;36(7):673-81.
21. Nagabhiru S. A prospective study of serum amylase levels in acute organophosphorus poisoning and its relationship with its severity and outcome. J Assoc Physicians India. 2020 Jan;68(1):102.
22. 0. Peter JV, Thomas L, Graham PL, Moran JL, Abhilash KPP, Jasmine S, et al. Performance of clinical scoring systems in acute organophosphate poisoning. Clin Toxicol. 2013;51(9):850-4. 23. Yoshida S, Okada H, Nakano S, Shirai K, Yuhara T, Kojima H, et al. Much caution does no harm! Organophosphate poisoning often causes pancreatitis. J Intensive Care. 2015;3(1):21.
24. Lyu CP, Pei JR, Beseler LC, Li YL, Li JH, Ren M, et al. Case control study of impulsivity, aggression, pesticide exposure and suicide attempts using pesticides among farmers. Biomed Environ Sci. 2018 Mar;31(3):242-246.
25. Sungur M, Guven M. Intensive care management of organophosphate insecticide poisoning. Crit Care. 2001 Aug;5(4):211-5.
26. Noshad H, Ansarin K, Ardalan MR, Ghaffari AR, Safa J, Nezami N. Respiratory failure in organophosphate insecticide poisoning. Saudi Med J. 2007 Mar;28(3):405-7.
27. Sivaganabalan R, Mohd Jamin Z, Loke KY, Z'aba N, Periathamby S. Retrospective observational study of organophosphate poisoning in an urban Malaysian Hospital. J Clin Toxicol. 2018;8(2):1-8.
28. Singh S, Bhardwaj U, Verma SK, Bhalla A, Gill K. Hyperamylasemia and acute pancreatitis following anticholinesterase poisoning. Hum Exp Toxicol 2007; 21(4):175- 7.
29. Aslan S, Cakir Z, Emet M, Serinken M, Karcioglu O,Kandis H et al. Acute abdomen associated with organophosphate poisoning. J Emerg Med 2011 ;41(5):507- 12.

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 08, 2023

30. Ghaniger M,Hemamalini G,Sanjana K. Prevalence of acute pancreatitis in organophosphate poisoning in correlation with elevated serum amylase and lipase level in a tertiary care hospital .Sch. J. Med.Sci.,2016;4:963-65.