ORIGINAL ARTICLE

HYPERAMYLAEMIA AND ACUTE PANCREATITIS FOLLOWING ORGANOPHOSPHATE POISONING

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ABSTRACT

Objective: To determine the frequency of hyperamylasemia and acute pancreatitis following organophosphate poisoning.

Methodology: This is a descriptive study conducted at the Medicine Department, Abbasi Shaheed Hospital Karachi during the period of six months from 16th June 2006 to December 2006. All patients of both sexes and ages above 15 years admitted with a positive history of organophosphate poisoning (OP) were included in the study. A special Proforma was designed to enter all the collected data containing the basic information about the patient, history of recent event and the past history, physical examination and the relevant investigations like complete blood count, serum amylase and lipase, alanine aminotransferase (ALT), lactate dehydrogenase (LDH) and ultrasound abdomen.

Result: Among 90 patients, hyperamylasemia was found in 28 (31%) patients. Hyperlipasemia was seen in nine (10%) patients and pancreatitis was seen in two (2.2%) patients.

Conclusion: Hyperamylasemia is more frequently seen in organophosphate poisoning while two patients proved to have acute pancreatitis as a complication.

KEY WORDS: Organophosphate Poisoning, Acute Pancreatitis, Hyperamylasemia, Hyperlipasemia.

INTRODUCTION

In Pakistan, the prevalence of depression is high and suicidal tendencies are increasing.1,2 Insecticide intake as a suicidal attempt has been seen very often in our society and in other developing countries as it is readily available in every home.3,4,5 Organophosphate compounds are diverse group of chemicals used in domestic and industrial settings. These compounds are possibly the most widely used insecticides in the world.5

The organophosphate intoxication can occur by suicidal and accidental means.6 The major effect of these agents is inhibition of acetylcholinesterase, a neurotransmitter found in the central and peripheral nervous system which causes over stimulation of muscaranic and
nicotinic receptors which results in wide spread clinical symptoms like bradycardia, hypotension, increased salivation, blurred vision, confusion etc.\textsuperscript{7,8}

World wide mortality studies report mortality rates of 3-25\% from organophosphate poisoning.\textsuperscript{9} Acute pancreatitis is one of the grave complications of this poisoning.\textsuperscript{9,11} It is thought to occur from ductal hypertension and pancreatic parenchymal injury.\textsuperscript{11-13} This potentially fatal complication can be overlooked in the absence of typical clinical features of acute pancreatitis.\textsuperscript{14,15}

There are few case series about this subject in the international literature, but it is believed that there are more cases than are reported for this condition. Although we come across a large number of patients with this poisoning now in our clinical practice, there is no local data available regarding the frequency of high amylase and lipase levels and this potentially grave complication of pancreatitis in pesticide poisoning.

Hyperamylasemia is frequently seen in organophosphate poisoning due to cholinergic stimulation of pancreas. It is hyperlipasemia which leads to the suspicion of acute pancreatitis.

This study was therefore designed to determine the frequency of hyperamylasemia and acute pancreatitis in organophosphate poisoning in our setup and to reduce mortality and hospital stay by its early detection.

**METHODOLOGY**

This is a descriptive case series study carried out in Abbasi Shaheed Hospital, Medical units I, II and III which is a thousand bedded tertiary care facility catering for acute and sub-acute emergencies. The study was conducted over a period of six months from June 16\textsuperscript{th} 2006 to Dec 16\textsuperscript{th} 2006.

Sample size was calculated according to standard formula \( Z^2 \times P \times (1-P)/C^2 \) which turn out to be 90. Confidence level was 95\%, confidence interval was 0.1 and percentage was 50. All patients including both sexes and ages above 15 years with a recent history of organophosphate ingestion, inhalation or cutaneous absorption with clinical sign and symptoms of organophosphate poisoning were included in the study.

Those patients with history of ingestion of any other material along with organophosphates, who were addicted to alcohol or had a history of gallstones or gallstones seen on ultrasound or any other history of gastric ulcer or burning epigastric pain in past were excluded from the study. Also those who had gone through ERCP (endoscopic retrograde cholangiopancreatography) in previous 24 hours or had a positive history of drug intake like azathioprine, mercaptopurine, asparginase, valproic acid, pentamidine, estrogens etc. were not included in the study.

Serum amylase and lipase levels were measured with a Hitachi-911 autoanalyser via enzymatic and colorimetric assay. Serum amylase levels between 0 and 95 u/l and serum lipase levels between 0 and 60u/l were accepted as normal. Patients with amylase levels between 100 and 300 u/l were accepted as possible pancreatitis, and only patients with concomitantly two fold elevated levels of lipase (above 60 u/l) were diagnosed as acute pancreatitis.

Complete blood count was obtained to observe any rise in leucocyte count. Alanine aminotransferase (ALT), lactate dehydrogenase and levels of glucose were also measured. Ultrasound abdomen was performed in all patients with raised lipase levels.

**Data Collection Procedure:** A special Proforma was designed to enter all the collected data containing the basic information about the patient, history of recent event and the past history, physical examination and lab investigations including complete blood count, random blood sugar, alanine aminotransferase (ALT), lactate dehydrogenase, serum amylase and lipase and ultrasound abdomen.

**Data Analysis:** The collected data was analyzed statically using SPSS version-10 on computer. Descriptive statistics like frequency and percentage of qualitative variables like sex, history, presenting complaints, clinical findings and causes of pancreatitis including gallstones, alcohol addiction, drug intake etc and quantitative variables like age, weight, amount of pesti-
cide ingestion, time of ingestion and stomach wash done were presented by mean and standard deviation.

**RESULTS**

During period of study 90 patients with ingestion of organophosphates were evaluated. Seventy one among 90 patients intended to commit suicide (78.8 %), whereas 19 patients, (21.2 %) were exposed to organophosphates due to accidental event. None came with a homicidal attempt.

Among 88 patients (97.7 %) were exposed to organophosphates through gastrointestinal route, two patients via inhalation (2.2 %), and none by cutaneous absorption. Among 90 patients sex distribution showed 54 patients (60 %) were females. Thirty six patients (40 %) were males. Male to female ratio was 1:1.5. Among 54 females 40 (74%) had intended suicidal attempt. Fourteen females (25.9%) gave statement of accidental intake of organophosphates. Among 36 males 31 (86.1%) males were exposed to organophosphates as a suicidal attempt and 5 (13.8%) were accidental. Mean age at presentation was 25 years. The youngest was 15 years old whereas the oldest was 40 years old.

Through the six months period 28 of 90 patients (31%) were found to have hyperamylasemia. Fifteen patients (16.6%) had more than threefold elevated amylase levels. Eleven had (12.2%) moderate hyperamylasemia and two (2.2%) had only borderline raised amylase levels.

Total nine patients (10%) out of 28 with hyperamylasemia, had raised lipase levels (>60 IU), among them seven had less than two fold elevation of lipase while two patients had two fold elevation of lipase with a four fold increase in a repeat sample after 30 hours. Eight of 28 patients with manifested hyperamylasemia > 300u/l and one of 28 patients with moderate hyperamylasemia (100-300 u/l) also had hyperlipasemia. Among 90 patients 28 with hyperamylasias invariably had raised leucocyte count, raised SGPT and LDH. (Table-I)

<table>
<thead>
<tr>
<th>Leucocyte (10 x 10^3 cmm^3) above</th>
<th>Normal Amylase Levels(&lt; 90 u/l) (No. of patients)</th>
<th>Serum Amylase Levels(90-100 u/l) (No. of patients)</th>
<th>Serum Amylase Levels(100-300 u/l) (No. of patients)</th>
<th>Serum Amylase Levels(&gt;300 u/l) (No. of patients)</th>
<th>Total (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leucocyte</td>
<td>12</td>
<td>2</td>
<td>11</td>
<td>15</td>
<td>44.4%</td>
</tr>
<tr>
<td>SGPT u/l (&gt;35)</td>
<td>2</td>
<td>2</td>
<td>11</td>
<td>15</td>
<td>33.3%</td>
</tr>
<tr>
<td>LDH u/l (&gt;450)</td>
<td>7</td>
<td>2</td>
<td>11</td>
<td>15</td>
<td>38.8%</td>
</tr>
</tbody>
</table>

Among the patients with normal amylase levels, isolated elevated leucocyte count was noted in 12 patients (13.3%), isolated raised LDH was found in seven patients (7.7%) and raised SGPT was seen in two patients (2.2%).

Among 90 patients the most common clinical presentation was excessive salivation seen in 42 (46.6%) of patients. Retching only was observed in 30 patients (33.3 %) while vomiting was seen in 22 (24.4%) of patients. Abdominal pain was seen in 20 patients (22.2%). Out of these five had hyperamylasemia and one had acute pancreatitis proven by raised lipase levels and ultrasound findings. Confusion and drowsiness was noted in 19 patients (21%).

The frequently observed clinical findings among 90 patients with a positive history of ingestion of organophosphates were constricted pupils seen in 58 patients (64.4%). Fasciculations were noted in 30 patients (33.3%). Chest crepitations were heard in 15 (16.6%). Respiratory depression was observed in 10 patients (11.1%). Convulsions were seen in two (2.2%). Among 90 patients 25 (27.7%) have no significant clinical finding on presentation. Three patients died during the study, two due to respiratory depression and one due to convulsions and aspiration.
DISCUSSION

Cases with acute pancreatitis as a complication of organophosphate exposure have been reported in the literature. The possible pathogenetic mechanism suggested for the pancreatic insult is excessive cholinergic stimulation of the pancreas and ductal hypertension.\(^\text{11,12}\) In Pakistan there is no study ever done to look for the frequency of hyperamylasemia and subsequent hyperlipasemia with an objective to detect pancreatitis which is an overlooked but serious complication of organophosphate poisoning.

Martin Rubi et al have reported only three patients with pancreatitis in a total number of 506 cases of organophosphate intoxication. This indicates a percentage of 0.59\%.\(^\text{16}\) Singh et al have reported 37 patients in whom serum amylase was found to be elevated out of 79 patients (46.95\%). But only one patient was proved to have pancreatitis making a percentage of 1.2\%.\(^\text{17}\) Lee et al reported 44 patients with hyperamylasemia in a group of 121 patients with organophosphate intoxication.\(^\text{14}\) Lipase was measured in 28 patients with hyperamylasemia and nine of 28 had hyperlipasemia. The finding of hyperamylasemia was closely related to clinical severity and presence of shock. This makes a percentage of 5.66\%. Sahin et al have reported acute pancreatitis in 6 patients among 47 making a percentage of 12.7\%.\(^\text{15}\) N Krupesh et al reported hemorrhagic pancreatitis in four patients among 62 making a percentage of 6.4\%, two of them died due to pancreatitis.\(^\text{18}\)

However in our study, we observed frequent hyperamylasemia in 31\% but subsequent hyperlipasemia was seen in 10\% and proven pancreatitis in 2.2\%. The subsets of patients with hyperlipasemia were considered for possible pancreatitis and were followed up accordingly. Total nine patients (10\%) had raised lipase levels (>60 IU), among them seven had less than two fold elevation of lipase while two patients had two fold elevation of lipase with a four fold increase in a repeat sample after 30 hours. Ultrasound abdomen showed swollen pancreas in these two patients while the ultrasound in the seven patients with borderline elevation of lipase showed altered echogenicity of pancreas and their lipase levels on repeat sample did not show rising levels. Ultrasound pancreas of these seven patients became normal when repeated after five days.

In this study the percentage of pancreatitis in our setup is lower as compared to the studies conducted internationally but higher in comparison with Martin Rubi et al\(^\text{16}\) and Singh et al.\(^\text{17}\) We found that elevation of serum amylase is common in patients with pesticide poisoning. However, acute pancreatitis is rare.

We also observed that those nine patients with hyperlipasemia had a delayed transportation to hospital. Time lapse between ingestion of insecticide and reaching to hospital and subsequent management was more than four hours as compared to those who had arrived to hospital within two hours. We have also observed elevation in the serum levels of SGPT, LDH and TLC in all patients showing raised amylase and lipase.

Limitation of our study was that serum cholinesterase levels were not done on admission because of non availability of test in our hospital lab and patients poor socioeconomic status did not allow us to get it done from other lab. The diagnosis of organophosphate poisoning was solely based on history and clinical examination at presentation.

CONCLUSION

Acute pancreatitis is a serious but seldom noticed complication of organophosphate intoxication. Amylase levels should be done in patients with high suspicion of pancreatitis. Those with elevated levels should undergo lipase estimation for confirmation of diagnosis and subsequent management. Since early detection and active intervention can save lives there should be more studies focused on this aspect of organophosphate poisoning.
Author’s Contributions: Ahmed. A was the major contributor in collecting data and writing the manuscript. Begum I, Aquil N and Atif S reviewed the manuscript and helped in processing the data. Hussain.T and Vohra. EA also contributed in reviewing and approving the manuscript for final publication.

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