GLYCEMIC CHANGES IN ACUTE ANTICHOLINESTERASE INSECTICIDE POISONING

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ABSTRACT

Background: Patients admitted with acute anticholinesterase poisoning were observed to manifest certain glycemic changes, albeit transient. This study was undertaken to elucidate these changes in detail.

Objective: To study the prevalence of any glycemic change in acute anticholinesterase insecticide poisoning and to establish their correlation, if any, with the severity of poisoning.

Methods: All patients admitted at our center with a confirmed diagnosis of acute anticholinesterase insecticide poisoning were included in the study. The presence of any glycemic change (hyperglycemia or hypoglycemia or ketosis or glycosuria) was noted and its magnitude and duration were recorded. The presence of any glycemic change was correlated with the severity of poisoning.

Results: Of the 76 patients studied, 39 (51%) had consumed organophosphate and 37 (49%) had consumed carbamate. Among the 39 organophosphate poisoning cases, glycosuria alone was observed in 22 cases (56.41%) and along with hyperglycemia in 8 cases. Among the 37 carbamate cases, 14 (37.84%) had glycosuria alone and 5 cases had hyperglycemia in addition. None had hypoglycemia or ketosis. However, the observed glycosuria was transient lasting for a mean of 2.75 days in organophosphate group and 2.25 days in carbamate group. Hyperglycemia lasted slightly longer with a mean...
duration of 3.25 days and 2.75 days in organophosphate and carbamate poisoning respectively. The glycemic changes observed occurred more frequently in patients with Bardin’s grade 2 and 3 poisoning.

**Conclusion:** Transient glycosuria with or without hyperglycemia occurred in a significant number of patients with organophosphate and carbamate poisoning. A positive correlation existed between the glycemic changes and the severity of poisoning. Long term clinical implications of these glycemic changes need to be further evaluated by follow-up studies.

**Keywords:** anticholinesterase poisoning, glycosuria, Hyperglycemia

**INTRODUCTION**

Organophosphates (OP) and carbamates first discovered more than 100 years ago are at present the predominant group of insecticides employed globally for pest control. These compounds are toxic to humans as well and represent an important source of suicidal poisoning in the present days. Acute anticholinesterase poisoning is one of the most common poisonings in some of the less-developed nations in South Asia.¹

In addition to increased cholinergic activity in acute anticholinesterase poisoning, there are a few glycemic changes seen which can lead to diagnostic confusion. Although mild glycemic changes do not offer a major obstacle during management of these cases, recent animal studies have shown increased glucose levels to exaggerate cholinergic changes.² All varieties of glycemic changes ranging from hypoglycemia to hyperglycemia and ketoacidosis have been reported, studies corroborating these findings are only few.³ ⁴ The present endeavor was undertaken to study the various glycemic changes in acute anticholinesterase poisoning.

**METHODOLOGY**

The prospective observational study was done in Tertiary care Hospital in Bangalore from January 2008 to December 2009. Patients aged over 18 years with a diagnosis of acute anticholinesterase poisoning were included in the study. The diagnosis was based on history of short term exposure or contact, characteristic clinical signs and symptoms, decrease in serum cholinesterase activity and improvement of the symptoms and signs after treatment with atropine and pralidoxime. Subjects wherein the exact nature of the poisoning could not be established and known diabetics were excluded from the study.

A detailed history including particulars regarding age sex, type of compound consumed, time-lag between consumption and initiation of treatment was taken followed by a thorough clinical examination. The
severity of the poisoning was graded on a scale of 0 to 3 based on the classification by Bardin et al.\textsuperscript{5}

At the time of admission, complete blood count, random blood sugar, urinalysis for glycosuria and ketone bodies, arterial blood gas analysis, serum pseudocholinesterase, serum amylase, renal and liver function tests were performed. Glycated haemoglobin levels were done to check for undiagnosed diabetics.

Hyperglycemia and hypoglycemia were defined as random blood glucose of more than 200 mg/dL and hypoglycemia as less than 60 mg/dL. Glycosuria was detected using ketodiastix strips. The magnitude of glycosuria was quantified as 0.25g\% (1\textsuperscript{+}), 0.5g\% (2\textsuperscript{+}), 1g\% (3\textsuperscript{+}) and >2g\% (4\textsuperscript{+}). The cases with hyperglycemia were meticulously tested at regular intervals until their blood sugars were normal. The duration of glycosuria was also similarly recorded. The presence of hyperglycemia or glycosuria or hypoglycemia or ketosis was correlated with the severity of the poisoning with respect to the nature of the compound consumed, the time lag between consumption and initial treatment, the clinical grade of poisoning, the serum pseudocholinesterase level and the requirement of assisted ventilation.

STATISTICAL ANALYSIS

Statistical analyses were performed using Statistical Package for Social Sciences (SPSS) for Windows 16.0 (SPSS Inc., Chicago, USA). The results for each parameter (numbers and percentages) for discrete data and average for continuous data are presented in tables and figures using Microsoft office 2007 software package. Chi square tests were used to analyze the significant difference between various groups. Two tailed ‘p’ values below 0.05 were considered significant.

RESULTS

There were 103 poisoning cases at our set-up during the study period. Of these, the exact type of the compound consumed was known only in 76 patients and were included in the study (table 1). 39 (51.32\%) had consumed OP compound and 37 (48.68\%) had consumed carbamate compound. Methylparathion was the commonest OP compound consumed and Carbaryl was responsible for most cases of carbamate poisoning. There was no significant association between glycemic changes with age or gender of the study subjects.

Glycosuria was noted in 22 cases of OP poisoning (56.41\%) and 14 cases of carbamate poisoning (37.84\%). Out of the 22 glycosuria cases, hyperglycemia was seen in 8 (20.51\%) of OP poisoning and 5 (13.51\%) of
carbamate poisoning cases (table 2). No significant difference existed between OP and carbamate compounds with respect to glycemic changes (p>0.05). Also, no compound in study resulted in more frequent glycemic changes than the others. Serum amylase was raised in 44% of OP cases and 12% of carbamate cases; however, there was no correlation between serum amylase and hyperglycemia in both OP and carbamate poisoning groups. Also, serum creatinine was raised in 8% of OP cases and 5% of carbamate cases and no correlation existed between raised serum creatinine and glycosuria in both groups.

The observed glycosuria was transient lasting for a mean of 2.75 days in OP group and 2.25 days in carbamate group. Hyperglycemia lasted slightly longer with a mean duration of 3.25 days and 2.75 days in OP and carbamate poisoning. The blood sugars at the time of discharge were found to be normal.

Also, glycosuria occurred more frequently in patients with grade 2 and 3 poisoning according to Bardin classification in OP compound poisoning; however, the same was not observed in carbamate group (Table 3). Glycosuria was noted to occur more frequently with a delay in treatment in patients poisoned by OP compound (p<0.05) but no such association was noted with carbamate poisoning (Table 4).

DISCUSSION

Few studies have highlighted the occurrence of glycosuria with or without hyperglycemia in most cases of anticholinesterase poisoning.\(^3\)\(^4\) The glycosuria was observed to be transient suggesting that it was a self-limited phenomenon. Poovala et al showed that OP poisoning could lead to acute tubular necrosis due to enhanced lipid peroxidation caused by reactive oxygen metabolites.\(^6\) However, they also noted that the renal toxicity was unrelated to OP-induced acetylcholinesterase inhibition. In the present study, we did not find any correlation between raised serum creatinine and glycosuria, indicating that the latter could not be explained exclusively by renal toxicity.

Liu and colleagues found that glucose feeding can markedly exacerbate the toxicity of the anticholinesterase insecticide, parathion in rats and was modulated by nitric oxide.\(^2\) Hyperglycemia has been reported many times in the literature and many mechanisms have been propounded in the pathogenesis of hyperglycemia following anticholinesterase compound poisoning. While one theory states marked catecholamine excess following continuous cholinergic stimulation induced by the poisoning, there are also experimental studies to suggest that persistent cholinergic spur could also stimulate ACTH release from the anterior pituitary.\(^7\)\(^8\) Hyperglycemia has been also attributed by increased glycogen
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breakdown. Finally, hyperamylasemia was seen accompanying hyperglycemia suggesting the possibility of pancreatitis as one of the mechanisms. We studied the relation between hyperglycemia and hyperamylasemia and found no correlation between the two.

Glycosuria was noted to occur more frequently with a delay in treatment in the present study. Although, we did not find any scientific documentation, the same could be explained by the increasing adrenaline excess following continuous cholinergic stimulation induced by the poisoning. Also the stress of the delay of treatment could contribute to the adrenaline gush and the associated hyperglycemia and glycosuria.

While animal studies have shown hyperglycemia to exaggerate cholinergic changes in acute anticholinesterase poisoning, similar findings in humans are not established. We observed the glycemic changes were more frequently seen with worsening grade of poisoning. Also, neither direct renal injury is solely responsible for glycosuria nor the hyperamylasemia wholly accounted for hyperglycemia. Further research is needed to shed light to the exact etiology for the hyperglycemia resulting in acute anticholinesterase poisoning and to see the impact of glycemic control over cholinergic toxicity.

Though diabetics were excluded, incipient diabetes could not be ruled out with certainty and posed as a limitation in this study.

CONCLUSION

Glycosuria with or without hyperglycemia occurred in a significant number of patients with acute anticholinesterase poisoning; these changes were however transient. A positive correlation existed between the glycemic changes and the severity of poisoning as determined by Bardin’s clinical grade and the time lag between consumption of poison and treatment. Impact of glycemic control on the severity of poison and long term implication of these glycemic changes needs to be further elucidated.

REFERENCES


Table 1: Gender-wise and compound-wise distribution of the study subjects

<table>
<thead>
<tr>
<th>Group</th>
<th>Males</th>
<th>Females</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>OP</td>
<td>24</td>
<td>15</td>
<td>39</td>
</tr>
<tr>
<td>Carbamate</td>
<td>23</td>
<td>14</td>
<td>37</td>
</tr>
<tr>
<td>Total</td>
<td>47</td>
<td>29</td>
<td>76</td>
</tr>
</tbody>
</table>

Table 1: The OP compound group, carbamate group and overall male: female ratio was 1.6:1, 1.64:1 and 1.62:1 respectively.

Table 2: Nature of anticholinesterase poisoning and the associated glycemic changes

<table>
<thead>
<tr>
<th>Group</th>
<th>Glycosuria</th>
<th>Hyperglycemic Glycosuria</th>
<th>Euglycemic Glycosuria</th>
</tr>
</thead>
<tbody>
<tr>
<td>OP (n=39)</td>
<td>22 (56.41)</td>
<td>8 (20.51)</td>
<td>14 (35.90)</td>
</tr>
<tr>
<td>Carbamate</td>
<td>14 (37.84)</td>
<td>5 (13.51)</td>
<td>9 (24.22)</td>
</tr>
<tr>
<td>Significance</td>
<td>p&gt;0.05</td>
<td>p&gt;0.05</td>
<td>p&gt;0.05</td>
</tr>
</tbody>
</table>

Table 2: There was no significant difference between OP and carbamate compound with respect to glycemic changes.
Table 3: Glycosuria in various grades of poisoning

<table>
<thead>
<tr>
<th>Grade</th>
<th>Total cases</th>
<th>OP poisoning</th>
<th>Glycosuria (%)</th>
<th>Total cases</th>
<th>carbamate poisoning</th>
<th>Glycosuria (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>16</td>
<td>4 (25.00)</td>
<td>27</td>
<td>7 (25.93)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>15</td>
<td>11 (73.33)</td>
<td>6</td>
<td>4 (66.67)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>8</td>
<td>7 (87.50)</td>
<td>4</td>
<td>3 (75.00)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Significance: P<0.001, p>0.05

Table 3: It was observed that the glycemic changes occurred more frequently with worsening grade of poisoning.

Table 4: Association between glycemic changes and time lag in the initiation of treatment

<table>
<thead>
<tr>
<th>Time Lag</th>
<th>&lt;3 hour</th>
<th>&gt;3 hour</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glycosuria with OP Poisoning (n=22)</td>
<td>7 (31.18)</td>
<td>15 (68.18)</td>
<td>p&lt;0.05</td>
</tr>
<tr>
<td>Glycosuria with carbamate poisoning (n=14)</td>
<td>5 (35.71)</td>
<td>9 (64.29)</td>
<td>p&gt;0.05</td>
</tr>
</tbody>
</table>

Table 4: While there was a significant increase in glycosuria with delay in treatment of OP poisoning, similar statistical significance was not noted in carbamate group.