Pralidoxime in Organophosphorus Poisoning

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ABSTRACT

Introduction: Pralidoxime are enzyme reactivator that are known to reactivate the phosphorylated acetylcholinesterase by binding to the organophosphorus molecule. The use of oximes in acute organophosphorus poisoning has been a controversial subjects for over two decades. This study was conducted with the objective to find out the estimation of serum cholinesterase and use of pralidoxime in organophosphorus poisoning.

Methods: A prospective analysis of all organophosphorus poisoning cases presented at the Emergency Department, Tribhuvan University Teaching Hospital for seven months was done.

Results: Out of 26 cases about 60% of poisoning cases were monitored for pseudocholinesterase level. About 50% of them had pseudocholinesterase level within normal limit and 20% had less than 10% of normal value. Only 33% cases with pseudocholinesterase level less than 10% were treated with pralidoxime.

Conclusions: The initial dose of Pralidoxime used was 1 gm followed by maintenance dose of 500mg 6 hourly, the doses prescribed were less than WHO recommended doses.

Keywords: cholinesterase, emergency, organophosphorus poisoning, Pralidoxime

INTRODUCTION

Poisoning is one of the common causes of hospitalization through emergency and is a major health problem in Nepal. Among the organophosphorus(OP) compounds, methyl parathion (Metacid) is the most commonly used agent.¹

Pralidoximes(PAM) are nucleophilic agents that are known to reactivate the phosphorylated acetylcholinesterase.²

The use of oximes in acute OP poisoning has been controversial. Initial uncontrolled studies suggested that oximes were useful in the routine management of OP poisoning.³

Current evidence is insufficient to indicate whether oxime is harmful or beneficial in the management of acute OP poisoning. A much large Randomized Controlled Trial is required to compare the WHO recommended pralidoxime regimen (more than 30 mg per kg bolus followed by more than 8 mg per kg per hour infusion) with placebo.⁴ Hence, the present study was

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conducted with the objective to find out the estimation of serum cholinesterase and use of pralidoxime in organophosphorus poisoning.

METHODS

A prospective, cross sectional study was done on cases attending the emergency department of TU Teaching Hospital, Kathmandu from June 15, 2006 to Jan 15, 2007.

The data was collected using interview and observation technique. Interview was conducted with patient or patient attendants using structured questionnaires. Similarly data were recorded using observation technique. Verbal consent of the patient or guardian was taken. All patients attending emergency were included in the study. All the OP poisoning cases were observed and documented. All the cases followed up till in the emergency room and outcome was documented.

Interview questionnaire included name of poison ingested, amount of poison, duration of poisoning and symptoms at presentation.

The observation was used to collect data on general and specific treatment given, serum pseudocholinesterase level, dose of pralidoxime and patients outcome.

After collecting the data, the variables were classified and tabulated. Similarly, data analysis and interpretation were done.

RESULTS

There were 26 patients of OP poisoning who attended the emergency room of the hospital. There were 14 males (53.9%) and 12 females (46.1%).

Fifteen cases (57.7%) were estimated for serum cholinesterase. Remaining did not get estimated because of inaffordability of estimation cost. (Table1).

Table 1. Estimation of serum cholinesterase

<table>
<thead>
<tr>
<th>Estimation</th>
<th>Number (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Estimated</td>
<td>15 (57.7)</td>
</tr>
<tr>
<td>Not estimated</td>
<td>11 (42.2)</td>
</tr>
</tbody>
</table>

Table 2. Values of serum cholinesterase

<table>
<thead>
<tr>
<th>Value</th>
<th>Number (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal (3500-8500)</td>
<td>8 (53.3)</td>
</tr>
<tr>
<td>Value more than 50% and less than 1 normal (1751-3499)</td>
<td>1 (6.7)</td>
</tr>
<tr>
<td>Value between 10 and 50% of normal (351-1750)</td>
<td>3 (20)</td>
</tr>
<tr>
<td>Value less than 10% of normal (350 or 3)</td>
<td>20</td>
</tr>
</tbody>
</table>

Seven cases (47%) had serum cholinesterase level below normal value. Twenty percent of cases had serum cholinesterase less than 10% of normal value (Table 2).

There were 17 cases who got PAM treatment, only 41.2% of them were estimated for serum cholinesterase and remaining cases were given PAM without estimation for serum cholinesterase (Table 3).

Table 3. PAM treatment receiving cases

<table>
<thead>
<tr>
<th>Serum cholinesterase</th>
<th>Number (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Estimated cases</td>
<td>7 (41.2)</td>
</tr>
<tr>
<td>Not estimated cases</td>
<td>10 (58.8)</td>
</tr>
</tbody>
</table>

There was only one case with serum cholinesterase less than 10% of normal value who got PAM treatment, the other two cases also had less than 10% but they did not get PAM treatment. There were three cases with serum cholinesterase level between 10-50% of normal value but only one of them received PAM. There was one case with serum cholinesterase more than 50% of normal value receiving PAM. On the other hand, out of eight cases with normal serum cholinesterase, four cases got PAM treatment (Table 4).

Table 4. PAM treatment receiving cases

<table>
<thead>
<tr>
<th>Serum cholinesterase</th>
<th>PAM treatment receiving cases</th>
<th>PAM treatment not receiving cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Less than 10% of normal</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>10-50% of normal</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>More than 50% and less than normal</td>
<td>1</td>
<td>-</td>
</tr>
<tr>
<td>Normal</td>
<td>4</td>
<td>4</td>
</tr>
</tbody>
</table>

Pralidoxime (PAM) was used in the dose of 1 gm bolus followed by 500 mg 4 to 6 hourly

DISCUSSION

Organophosphorous (OP) compound has been found to be the commonest poisons and among the OP compound, methyl parathion (Metacid) is commonly used agent in Nepal.

The present study has been conducted to find out the serum cholinesterase estimation and use of PAM in OP poisoning in TU Teaching Hospital Emergency.

The toxic mechanism of OP poisoning is based on the irreversible inhibition of acetylcholinesterase (AchE) due to phosphorylation of the active site of the enzyme. This leads to accumulation of acetylcholine and subsequent over-activation of cholinergic receptors at the neuromuscular junction and in the autonomic nervous systems. The rate and degree of AchE inhibition differs according to the structure of the OP compounds and the nature of their metabolites. Although
true cholinesterase level correlate with severity at presentation, pseudocholinesterase level do not. A 25% of greater depression in RBC cholinesterase level has been taken as the best indicator of OP poisoning.

Though there are controversies about the correlation between plasma cholinesterase activity and the severity of poisoning, it is a marker of the organophosphorus intoxication.

Pseudocholinesterase level below 10% of normal value has been associated with poor prognosis and increased mortality.

Studies have shown that cholinesterase enzyme reactivator like PAM has its role in reactivating this enzyme and its benefit is more pronounced if given in less than 12 hours of ingestion of poisoning.

The usefulness of oxime has been challenged over the past 20 years by physicians in many parts of the world. Current evidence is insufficient to indicate whether oxime is harmful or beneficial in the management of acute organophosphorous poisoning. A much large Randomized Controlled Trial is required to compare the WHO recommended pralidoxime regimen (more than 30 mg per kg bolus followed by more than 8 mg per hour infusions) with placebo.

In this study about 60% cases were estimated for serum cholinesterase level, remaining cases did not get estimated because of insufficiency of estimation cost. Among cholinesterase estimated patients about 50% had enzyme level below normal.

This study highlights the situation of serum cholinesterase enzyme estimation and the dose of PAM in the treatment of organophosphorus poisoning.

CONCLUSIONS

This study showed that 20% cases had pseudocholinesterase level less than 10% of normal value. The initial and maintenance dose of PAM used in all cases of OP poisoning were less than WHO recommended dosage.

REFERENCES