Adherence to the National Guidelines on the Management of Organophosphorus Poisoning

Jayasinghe SS¹, Fernando A¹

¹Department of Pharmacology, Faculty of Medicine, University of Ruhuna, Galle, Sri Lanka

Correspondence: Dr. S.S. Jayasinghe (sudheerasf@yahoo.com)

Source of funding: This study was supported by Wellcome Trust and NHMRC International Collaborative Research Grant (GR071669MA).

Conflicts of interest: The authors declare that there are no conflicts of interest.

ABSTRACT

Background: The National Guidelines on the Management of Organophosphorus (OP) poisoning include resuscitation, gastric lavage, administration of atropine and pralidoxime. Atropine should be commenced in the presence of cholinergic features and maintained to reverse them. Pralidoxime therapy in OP poisoning should be continued until clinical recovery or seven days, whichever is longer. The aim of this study was to explore the adherence to the National Guidelines on atropine and pralidoxime in OP poisoning in two selected hospitals in the Southern province.

Materials: A cross sectional survey was conducted at the Teaching Hospital, Galle and the General Hospital, Matara between June 2008 and September 2009. The details of administration of atropine, atropine adequacy during the therapy and pralidoxime were collected.

Results: A total of 149 patients were recruited. Eighty (54%) patients were direct admissions to the collaborating hospitals. Among them, 35 (44%) did not have cholinergic features at the time of presentation to hospital and 32 patients were treated with atropine before the appearance of cholinergic features. Seventeen (12%) patients neither showed features of atropine toxicity nor inadequacy. The number of patients who developed features of atropine toxicity and inadequacy in the two hospitals were 109 (73%) and 11 (7%), respectively. Seventy-eight (52%) patients did not receive the loading dose while 39 (26%) did not receive the maintenance dose of pralidoxime respectively. None of the patients received pralidoxime for the recommended duration.

Conclusions: Atropine was commenced in some patients without cholinergic features. Majority of the patients received toxic doses of atropine. None of the patients received the maintenance therapy of pralidoxime for the recommended duration. Further education of ward staff on the management of OP poisoning may be required.

Keywords: Atropine, organophosphorus compounds, patient care management, poisoning, pralidoxime compounds

Introduction

Acute pesticide poisoning is a major health problem especially in developing countries. It was estimated that one million serious, unintentional poisoning occurred and an additional two million people were hospitalized for attempted suicide with pesticides annually (1). In Sri Lanka, the majority of poisoning cases are self inflicted and 77% of the cases are in the age range of 11-30 years (2). Organophosphorus (OP) compounds were involved in 76% of pesticide poisoning (3).

Management of poisoned patients is challenging due to lack of specialized units, trained staff, equipments to deal with very sick patients, intensive care beds and ventilators (4). Further, the evidence for treatment is not satisfactory, drugs being either
poorly used or unavailable (4). The aim of this study was to explore the adherence to existing guidelines on atropine and pralidoxime therapy in the management of OP poisoning laid down by the National Poisons Information Center, National Hospital of Sri Lanka.

The current standard treatment for OP poisoning includes resuscitation, oxygen, atropine, oxime and diazepam. Despite the beneficial effects of pralidoxime with certain OPs, its effectiveness has not yet been clearly shown (5). Therefore atropine is the mainstay of treatment in OP poisoning.

**Administration of atropine**

The aim of early atropine therapy is to reverse the cholinergic syndrome and to improve cardiac and respiratory function as early as possible (4). Atropine dosing is aimed to keep the pulse rate more than 80 per minute, systolic blood pressure more than 80 mmHg and reversing bronchospasm and bronchorrhoea. The starting dose of atropine is 1 - 3 mg intravenously (IV) in to a fast flowing IV drip (6,7). Double the dose and continued to double each time if there is no response within 5 minutes after administration of atropine. Once the patient is atropinized (clear lungs, heart rate >80 bpm, systolic blood pressure >80 mmHg, dry skin and pupils no longer pin point) 10-20% of the total amount of atropine that was required to load the patient needs to be administered hourly. If the patient develops atropine toxicity (agitation, confusion, urinary retention, hyperthermia, bowel ileus and tachycardia) the infusion has to be stopped and restarted at 70-80% of the previous rate once features of toxicity have settled. The patient should then be frequently monitored and the infusion titrated to prevent features of atropine toxicity or the reappearance of cholinergic features (8).

**Administration of pralidoxime**

The loading dose of pralidoxime should not be given rapidly as it can cause vomiting (risk of aspiration), tachycardia, and diastolic hypertension (4). The current guidelines state that pralidoxime should be administered in a loading dose of 30 mg/kg over 20-30 min followed by 8-10 mg/kg per hour until clinical recovery (12-24 hours after atropine is no longer required or the patient is extubated) or seven days, whichever is longer (8). Less severely poisoned patients can be given 1g six hourly by slow IV bolus over 10-20 min (6). Pralidoxime is said to be effective if given within 24 hours (9).

The aim of this study was to explore the adherence to the National Guidelines on atropine and pralidoxime treatment in OP poisoning.

**Materials**

A cross sectional survey was conducted in the Teaching Hospital, Galle and the General Hospital, Matara between June 2008 and September 2009, with the approval of the Ethical Review Committee, Faculty of Medicine, University of Ruhuna, Galle.

Details of administration of atropine and pralidoxime were collected. Details of atropine adequacy during the treatment were also looked into.

The data collection and the monitoring of the patients were done by the Clinical Research Assistants (pre-intern medical graduates). The data were obtained from the bed head tickets, monitoring sheets, clinical examination of the patients and inquiring from the patients and the caregivers.

**Results**

A total of 149 (males 117) patients were recruited for the study. The median (inter quartile range) age of the patients was 34 (24 - 47) years. Except for one patient who had occupational exposure all others were suicidal attempts. Eighty (54%) patients were direct admissions to the collaborating hospitals whereas the rest of the patients were first admitted to the peripheral hospitals and then transferred. The patients reached the hospital within a mean (SD) of 6.4 (2.7) hours of ingestion. Table 1 shows the outcome following hospital admission. Twenty (13%) patients required admission to the Intensive Care Units. Eight of these patients died and the outcome was not known in the five patients who were transferred to the ICUs at other hospitals.

Among the 80 patients who had direct admission to the collaborating hospitals, 35 (44%) patients did not have cholinergic features (at least one feature; bronchorrea / bronchospasm, hypotension, bradycardia or excessive sweating) at the time of presentation to hospital and 32 patients were treated with atropine before the appearance of cholinergic
features. The prevalence of cholinergic features after OP ingestion is shown in Figure 1. Sixty eight (80%) patients who were directly admitted to the collaborating hospitals received a loading dose of atropine. From the total of 149 patients, 140 patients received a maintenance dose of atropine.

Seventeen patients showed neither features of atropine toxicity nor inadequacy. One hundred and nine patients (73%) developed features of atropine toxicity (at least one feature; agitation, confusion, urinary retention, hyperthermia, bowel ileus or tachycardia) and 11 (7%) patients showed evidence of atropine inadequacy (at least one feature; bronchorrhea / bronchospasm, hypotension, bradycardia, excessive sweating). Data of 12 patients were not sufficient to determine the adequacy of atropine.

Among the features of atropine toxicity tachycardia was the most prevalent feature (Figure 2). Thirty eight patients were not catheterized. Eight patients out of these 38 patients developed urine retention during atropine therapy.

Figure 3 shows the prevalence of features of atropine adequacy.

Table 2 shows the number of patients receiving loading and maintenance doses of pralidoxime. Five patients who did not receive pralidoxime, presented to the hospital after 24 hours of ingestion. The patients received 1-2 g of a loading dose of pralidoxime followed by a maintenance dose of 8-10 mg/kg/hr, for a mean duration of 1.3 (0.7) days. Five patients received only a single dose of maintenance therapy of pralidoxime whereas the maximum duration the patients received the maintenance dose of pralidoxime was 4 days.

Table 1: Outcome following hospital admission

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Number (%)</th>
</tr>
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<tbody>
<tr>
<td>Live</td>
<td>113 (76%)</td>
</tr>
<tr>
<td>Death</td>
<td>23 (16%)</td>
</tr>
<tr>
<td>Left against medical advice</td>
<td>8 (5%)</td>
</tr>
<tr>
<td>Transferred to ICU at other hospitals</td>
<td>5 (4%)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>149</strong></td>
</tr>
</tbody>
</table>

![Figure 1: Prevalence of cholinergic features](image)
Figure 2: Features of atropine toxicity

Figure 3: Adequacy of atropine therapy
Discussion

Atropine was commenced in some patients without cholinergic features. Majority of the patients received toxic doses of atropine. None of the patients received the maintenance therapy of pralidoxime for the recommended duration.

It was not recommended to commence atropine in OP poisoning in the absence of cholinergic features. Some patients presented to hospital soon after the ingestion before the appearance of cholinergic features. Pro-poison OP is converted to the active form as a fat soluble OP (eg. Fenthion) and released slowly from fat stores into the blood. In such situations careful observation is required to identify the development of the cholinergic features. But in busy medical wards it would be difficult to observe this continuously. Hence it may be considered rational to start atropine before the appearance of cholinergic features, if the ingestion can be confirmed, in order to prevent the occurrence of dangerous cholinergic effects.

In General Medical wards the maintenance dose of atropine is administered to patients via an intravenous drip set. Neither burette set nor infusion pump is used. Although the drip rate is adjusted, it is not protected. The position of the wheel in the intravenous drip set used for adjusting the rate may change position with patient movement and rapid flow through is possible, causing features of atropine toxicity. Frequent monitoring should be done and the drip rate adjusted according to the cholinergic features.

Oximes directly bind to and inactivate OP molecules. They accentuate the pharmacological activity of atropine and may be atropine sparing (10). The clinical usefulness of oxime therapy in OP poisoning is currently not clear. Patients poisoned with some OPs, those with dimethyl or S-alkyl chemical groups attached to the phosphate ion may not get a benefit from oximes (4.11). But patients poisoned with diethyl OPs are more likely to be benefited (4). A clinical trial conducted in Sri Lanka with 45 patients did not show any benefit from pralidoxime plus atropine over atropine alone in the management of OP poisoning (10). A study conducted in Vellore, India showed that low-dose infusion of pralidoxime caused harm (12). However, the National Guidelines recommend pralidoxime in OP poisoning. It was surprising why none of the patients received pralidoxime for the recommended duration.

Management of poisoned patients according to the guidelines, titrating the dose according to the clinical features and availability of antidotes at all times may not be possible in busy General Medical wards. Establishment of separate units to manage poisoning patients may improve the quality of management and outcome of the patients. It may be useful to launch Continuous Medical Education programs for the heath care staff in hospitals with regard to the management of poisoning.

Acknowledgements

We would like to thank the participants, the consultants who gave access to their patients, administrative staff and health care professionals at the Teaching Hospital, Galle and the General Hospital, Matara, Heads and staff members of the Department of Pharmacology and the Department of Medicine, Faculty of Medicine, University of Ruhuna, and the members and Clinical Research Assistants of the South Asian Clinical Toxicology Research Collaboration. A special word of thanks is extended to Professor NA Buckley, Professor AH Dawson, Professor KD Pathirana, and Professor PLAriyananda.

Source of funding

This study was supported by the Welcome Trust and a NHMRC International Collaborative Research Grant (GR071669MA).

Table 2: Receiving of loading and maintenance doses of pralidoxime

<table>
<thead>
<tr>
<th>Status</th>
<th>Loading dose</th>
<th>Maintenance dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Received</td>
<td>52 (35%)</td>
<td>85 (57%)</td>
</tr>
<tr>
<td>Not received</td>
<td>78 (52%)</td>
<td>39 (26%)</td>
</tr>
<tr>
<td>Data not adequate</td>
<td>19 (13%)</td>
<td>25 (17%)</td>
</tr>
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</table>
References


