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Original Article

Clinical study of continuous micropump infusion of atropine and pralidoxime chloride for treatment of severe acute organophosphorus insecticide poisoning

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Abstract

Background: Our study sought to assess the effectiveness of a constant micropump infusion of atropine and pralidoxime chloride compared with repeated-bolus doses in patients with severe acute organophosphorus insecticide poisoning (AOPP).
Methods: A total of 60 patients with severe AOPP, defined as cholinergic crisis with respiratory failure or cerebral edema, were randomly divided into two groups of 30 patients each. In the experimental group, patients received a continuous micropump of atropine and pralidoxime chloride; in the control group, patients were given intermittent injections of atropine and pralidoxime chloride. Primary outcome measures were the dose of atropine required for atropinization, Acute Physiology and Chronic Health Evaluation II (APACHE II) score at atropinization, time to atropinization and acetylcholinesterase (AchE) recovery time. Additionally, the case fatality rate was measured as a secondary outcome.
Results: Compared to patients in the control group, the time to atropinization, AchE recovery time, dose of atropine when atropinization occurred, and APACHE II score in the experimental group showed a statistically significant therapeutic effect ($p < 0.05$), and the case fatality rate of the experimental group was lower than that of the control group ($p < 0.05$).
Conclusion: Continuous micropump of atropine and pralidoxime chloride combined is more effective than the use of repeated-bolus injection in the treatment of severe acute organophosphorus insecticide poisoning.

Keywords: atropine; organophosphorus poisoning; pralidoxime chloride

1. Introduction

Acute organophosphorus insecticide poisoning (AOPP) is a major cause of self-poisoning in developing countries, responsible for the deaths of an estimated 200,000 people each year.[1] It is a common emergency accident in China with an average mortality rate of 10%. Furthermore, severe AOPP rapidly leads to acute cholinergic crisis and includes symptoms resulting from hyperstimulation of the central and peripheral muscarinic and nicotinic receptors. Death is usually caused by respiratory failure resulting from paralysis of the diaphragm and intercostal muscles and cerebral edema, with a case fatality rate of up to 30%.[2] The standard treatment for AOPP is to give intravenous atropine and oximes.[3] Treatment with atropine is well established, which inhibits the effect of acetylcholine at muscarinic receptors. It has been reported that continuous micropump injection of atropine can significantly reduce the case fatality rate of severe AOPP.[4] Reactivation of inhibited acetylcholinesterase (AchE) occurs after treatment with oximes, such as pralidoxime chloride, and the minimum concentration in plasma at which this treatment is effective is

Conflicts of interest: The authors declare that there are no conflicts of interest related to the subject matter or materials discussed in this article.

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thought to be 4 mg/L. A dose of 1 g of oximes every 4–6 hours has been the standard regimen in Asian district hospitals, but many clinicians remain unconvinced of its effectiveness.[5] Evidence suggests, however, that the concentration of pralidoxime in the blood might need to be higher to antagonize the toxic effects of many insecticides. Thus, a bolus-loading infusion followed by a maintenance infusion may be the best regimen. Because the study of continuous micropump infusion of oxime in treating AOPP has rarely been reported,[6] the effect of a continuous micropump of atropine and pralidoxime chloride combined in the treatment of severe AOPP has not been tested. In the current study, we aimed to assess the effectiveness of a constant micropump infusion of atropine and pralidoxime chloride compared with repeated-bolus doses in patients with severe AOPP.

2. Methods

2.1. Patients

Patients were enrolled in our study from July 2007 until May 2012. A total of 60 patients received a diagnosis of severe AOPP based on a history of oral consumption of organophosphorus insecticide, the presence of characteristic signs of acute cholinergic crisis (in particular: sweating, pinpoint pupils, urinary and fecal incontinence, bronchorrhoea, bronchospasm, and hypotension) with respiratory failure or cerebral edema, and plasma erythrocyte AchE activity less than 30% of normal. Exclusion criteria consisted of patients who received cardiopulmonary resuscitation during emergency admission, the presence of chronic disease such as heart and lung disease, and concomitant ingestion of other toxicants. Sixty patients with severe AOPP were randomly divided into a continuous micropump atropine and pralidoxime chloride group (experimental group) and an intermittent injection of atropine and pralidoxime chloride group (control group).

This research was approved by the Ethics Committee of The Songjiang Central Hospital and was undertaken in accordance with the principles of the Declaration of Helsinki.

2.2. Treatment

2.2.1. General supportive treatment

All patients with AOPP were assessed and resuscitated in the emergency room before admission to the intensive care unit. Sixty patients received intratracheal intubation and mechanical ventilation in order to maintain airway patency and ensure adequate arterial oxygen saturation. According to the standard treatment plan in China,[7–9] gastric lavage with 20,000 mL of warm water was immediately performed after intubation until the returning fluid was clear and odorless. After gastric lavage, crushed tablets of activated charcoal were left in the stomach and replaced every 8 hours for the next 48 hours. Meanwhile, every patient also received supportive treatment such as hepatoprotection (daily 1.8 g of reduced glutathione), rehydration, diuresis, and hemoperfusion (run immediately after admission, 2 hours daily for 2 days). Patients were monitored continuously by noninvasive means to measure their blood pressure, heart rate, respiratory rate, and arterial oxygen saturation.

2.2.2. Specific antidotal treatment

Every patient was given an initial loading dose of 20 mg of atropine and 2 g of pralidoxime chloride intravenously.[8,10] After the loading dose of atropine and pralidoxime chloride was administered in the experimental group, a continuous micropump atropine infusion was set up at a speed of 20 mg/hour to keep the patient atropinized without reaching toxic levels, using frequent adjustments of dose (usually adjusting the dosage every 5 minutes with the rate of 2 mg/hour declining according to the clinical symptoms of patient). When the patient achieved most of (at least 4 out of 5) the target endpoints[11] (i.e., heart rate > 80 beats/minute, dilated pupils, dry axillae, systolic blood pressure >80 mmHg, clear chest with absence of wheeze) for atropine therapy, an intravenous infusion of the minimum dose of atropine was maintained. Meanwhile, a continuous micropump of pralidoxime chloride infusion was also set up at a speed of 8 mg/kg/hour[10] until the AchE value recovered to 60% of normal.

In the control group, a subsequent dose of 5 mg of atropine injection every 10 minutes was given until atropinization was achieved. Patients also received an intravenous dose of 1 g of pralidoxime chloride every 6 hours until the AchE value recovered to 60% of normal.

2.2.3. Outcomes

The primary outcomes were the atropine dose needed for atropinization, the time to atropinization, the time to AchE recovery, and the Acute Physiology and Chronic Health Evaluation II (APACHE II) score at atropinization. Case fatality rate in the whole hospitalization period was considered a secondary outcome.

2.3. Statistical analysis

All analyses were performed using SPSS 11.0 software (SPSS Inc, USA). Continuous variables were investigated for departure from normality by use of the Shapiro–Wilk test. For the normally distributed data, we calculated the mean difference and performed Student t tests to compare the experimental group and the control group. For the skewed data, we performed nonparametric Mann–Whitney U tests to investigate differences between the two groups. The significance of the case fatality rate difference between two groups was determined by a Chi-square test, and $p < 0.05$ was used to determine statistical significance.

3. Results

There were a total of 60 patients including 28 men and 32 women with a mean age of 32.5 years, and an age range of 14–56 years. Among the 60 cases of poisoning, there were 18 cases of methamidophos, 17 cases of omethoate, 11 cases of dichlorvos, 5 cases of trichlorfon, and 9 cases of composite