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Efficiency of anisodamine for organophosphorus-poisoned patients when atropinization cannot be achieved with high doses of atropine

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ABSTRACT

Poisoning by organophosphorus insecticides is a major global public health problem. Although atropine has been widely used to treat organophosphate (OP) poisoning, sometimes atropinization cannot be achieved, even with high doses of atropine. Hence, we aimed to assess the effect of anisodamine for organophosphorus poisoned patients for whom atropinization could not be achieved through high doses of atropine. In this study, sixty-four OP-poisoning patients, all of whom accepted routine treatments but who did not attain atropinization after high doses of atropine for 12 h, were enrolled. The result showed that the time to atropinization was 24.3 ± 4.3 h in the anisodamine group, significantly shorter than in the atropine group (29.2 ± 7.0 h, $p < 0.05$); the hospital stay in the anisodamine group was 5.3 ± 2.5 days, significantly shorter than the 6.9 ± 2.3 days needed by the atropine group ($p < 0.05$). We draw a conclusion that anisodamine can shorten the process of atropinization and hospital stay in organophosphorus poisoned patients for whom atropinization cannot be achieved with high doses of atropine.

1. Introduction

Organophosphate (OP) poisoning is a life-threatening condition that is responsible for severe clinical emergencies throughout the world (Jeyaratnam, 1990; Moghadamnia and Abdollahi, 2002; Rahimi et al., 2006). An estimated 750,000 to 3 million people are deliberately (including suicide) or accidentally poisoned by organophosphate chemicals per year, with an estimated 300,000 deaths (Eddleston et al., 2005).

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Clinical manifestations of OP poisoning include cholinergic syndromes, central nervous system disorders, and cardiovascular disorders (Paudyal, 2008).

Following decontamination, depending on the severity of intoxication, the administration of atropine to counteract muscarinic over-stimulation, and an oxime to reactivate acetyl cholinesterase are indicated (Bajgar, 2004). Though the effectiveness of oximes in treating human OP poisoning is still debated, atropine is considered a significant cornerstone in the treatment of this intoxication (Husain et al., 2010; Eddleston et al., 2004; Balali-Mood and Saber, 2012). However, no consensus has been achieved on guidelines for atropine administration, with consequent wide variation in recommendations for atropine dosage (Perera et al., 2008).

In the clinic, it is very difficult to achieve atropinization for some organophosphorus victims, even with high dosage of atropine, and total doses as high as 116,000 mg atropine have previously been reported in the treatment of such patients (Karakus et al., 2012). On the contrary, some studies suggest that the use of high doses of atropine provides no therapeutic advantage to these patients (Eddleston et al., 2008). In the present study, we consider whether these victims could benefit from treatment with anisodamine.

2. Materials and methods

2.1. Study population

A retrospective chart review, covering January 1, 2005 to December 31, 2012, revealed a total of 64 OP poisoning patients who had accepted high doses of atropine. All of the patients had presented to the First Affiliated Hospital of Guangxi Medical University, and the Second Affiliated Hospital of Guangxi Liuzhou Technical Medical College in Guangxi, China. The subjects consisted of 26 (40.6%) males and 38 (59.4%) females, ranging in age from 17 to 59 years, with a mean age of 35.7 ± 10.0 years. This retrospective study was approved by the Ethics Committee of Guangxi Medical University and Guangxi Liuzhou Technical Medical College. Permission was similarly obtained from the hospital director to allow us to access the information from the patients' case notes, strictly for the purpose of this research.

2.2. Inclusion and exclusion criteria

Criteria for inclusion were: (1) diagnosis of OP poisoning (SSWAHS, 2007); (2) patient acceptance of routine treatments, including gastric lavage, atropine, pralidoxime, and supportive therapy; and (3) complete data.

Criteria for exclusion were: (1) complication due to exposure to another type of poison; (2) malignant tumor, psychosis, or serious primary disease of the liver, kidney, or hematopoietic system; and (3) premature termination of treatment.

2.3. Methods

All of the patients accepted routine treatments (gastric lavage, pralidoxime, atropine, and supporting treatment), but after treatment with high doses of atropine for 12 h, atropinization was still not achieved. The patients were divided into two groups according to the type of follow-up treatment. The first group, comprising 36 patients, continued with the original atropine-based treatment program. The second group, comprising 28 cases, switched to anisodamine after the initial, unsuccessful, 12-h treatment with atropine. Demographic characteristics, route of poisoning, organophosphate type, presentation time, clinical features, severity of intoxication, time until acetylcholinesterase (AChE) recovery, time to atropinization, treatment efficiency, complications, and hospital stay were compared between the two groups.

2.4. Definitions

(1) *Presentation time*: the duration from OP intake to admission.
(2) *Atropinization*: abatement of muscarinic signs such as miosis, diarrhea, vomiting, sweating, and bronchial secretions (SSWAHS, 2007).
(3) *High doses of atropine*: 5 mg intravenous (IV) atropine for every 3 min; the recommended dosage of atropine is 2–5 mg IV for every 3–5 min, so the definition of high dosage used in this study represents the highest end of the recommended range (SSWAHS, 2007).
(4) Severity of OP intoxication was graded as shown in Table 1 (SSWAHS, 2007).
(5) *Dosage and administration of anisodamine*: 10 mg IV for every 5 min (Ye et al., 2013).

2.5. Statistical analyses

Mean and standard deviation was used for the analysis of quantitative variables. Differences in age, presentation time, time until AChE recovery, time to atropinization, pralidoxime dose, atropine dose, and hospital stay were compared between the two groups by t-test. A chi-square test (χ^2-test) was used to evaluate differences in qualitative categories: gender, route of poisoning, organophosphate type, clinical features, severity of intoxication, treatment efficiency, and complications. A two-tailed p value less than 0.05 was considered statistically significant. All statistical analyses were carried out using the statistical software package SPSS 16.0 (SPSS Inc., Chicago, IL).

3. Results

As shown in Table 2, all 64 patients were poisoned by oral intake. There were no significant differences in gender, age, route of poisoning, organophosphate type, presentation time, clinical features, severity of intoxication, time until AChE recovery, treatment efficiency, or complications between the two groups ($p > 0.05$ for all). The time to atropinization was 24.3 ± 4.3 h in the anisodamine group, and this was significantly shorter than the 29.2 ± 7.0 h required by the atropine group ($p < 0.05$). The hospital stay in the anisodamine group was also significantly lower than that of the atropine group; 5.3 ± 2.5 days for the anisodamine group, compared with 6.9 ± 2.3 days for the atropine-only group ($p < 0.05$).