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Original Article

# The effectiveness of patient-tailored treatment for acute organophosphate poisoning


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ABSTRACT

*Background:* To determine a new pralidoxime (PAM) treatment guideline based on the severity of acute organophosphate intoxication patients, APACHE II score, and dynamic changes in serum butyrylcholinesterase (BuChE) activity.

*Methods:* This is a randomization trial. All patients received supportive care measurements and atropinization. Each enrolled patient was treated with 2 gm PAM intravenously as the loading dose. The control group was treated according to the WHO's recommended PAM regimen, and the experimental group was treated according to their APACHE II scores and dynamic changes in BuChE activity. If a patient's APACHE II score was ≧26 or there was no elevation in BuChE activity at the 12th hour when compared to the 6th, doses of 1 g/h PAM (i.e., doubled WHO's recommended PAM regimen) were given. The levels of the serum BuChE and red blood cells acetylcholinesterase and the serum PAM levels were also measured.

*Results:* Forty-six organophosphate poisoning patients were enrolled in this study. There were 24 patients in the control group and 22 patients in the experimental group. The hazard ratio of death in the control group to that of the experimental group was 111.51 (95% CI: 1.17–1.613.45; $p = 0.04$). The RBC acetylcholinesterase level was elevated in the experimental group but was not in the control group. The experimental group did not exhibit a higher PAM blood level than did the control group.

*Conclusion:* The use of PAM can be guided by patient severity. Thus, may help to improve the outcomes of organophosphate poisoning patients.

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## At a glance commentary

### *Scientific background on the subject*

The use of pralidoxime in the treatment of organophosphate poisoning is still under investigations. Studies have shown that a higher mortality was observed among severe intoxicated patients with the convention treatments. Therefore, it is required to treat the patients according to their organophosphate intoxicated severity.

### *What this study adds to the field*

This study found that the severity index, such as APACHE score, can be a guide for designing pralidoxime dose. Better patient outcomes were observed when treated according to their organophosphate intoxicated severity. The findings suggest an innovative tailored-made treatment protocol to organophosphate intoxicated patients in the future emergency medicine practice.

Acute pesticide poisoning is a major global health problem across the world [1,2]. In Taiwan, organophosphate intoxication accounted for 26.97% of all of the pesticide poisonings [3]. Acute respiratory failure and even death are quite common outcomes of acute organophosphate (OP) poisoning [4]. PAM has been used as an antidote for the treatment of acute OP poisoning patients; however, its use remains controversial [5–7]. The WHO's recommended PAM regimen (in adults, 30 mg/kg bolus, followed by a continuous infusion of 8 mg/kg/h to rapidly achieve and maintain a concentration of PAM above 4 mg/L) is based on animal studies [8]; moreover, the type of OP pesticide and the poisoning dosage influence the effects of treatment with PAM [9–14]. Thus, the clinical presentations and severity of OP poisoning may be complicated, and the effectiveness of PAM treatment requires re-examination.

According to the available literature, the acute physiology and chronic health evaluation II (APACHE II) score and serial cholinesterase changes are two OP poisoning severity assessment tools [15–17]. Higher mortality rates were observed among those with higher APACHE II scores in previous studies [15,16]. Increasing patient mortality rates was associated with the absence of elevating butyrylcholinesterase (BuChE) activity within 48 h of poisoning although they were treated with the similar PAM dosages. [17] Therefore, it seems reasonable that these effects may be linked to PAM dose prescriptions.

Based on the hypothesis that PAM dosages should be determined according to the severity of acute OP poisoning, this study aimed to examine the effectiveness of tailored treatment for acute organophosphate poisoning patients. Therefore, this study assessed a new PAM dosage regimen that is based on the severity of acute OP poising (i.e., APACHE II score) and dynamic changes in serum BuChE activity. Serum PAM concentrations, the changes of serum BuChE and red blood cell AChE (RBC AChE) activities were also measured to investigate how these factors were related to the prognosis and toxicokinetics of acute organophosphate poisoning patients.

## Methods

### *Study design and patient population*

This study received the approval of our local ethics committee (97-2306A3), and written informed consent was obtained from each patient or their closest relatives. This study was a randomized open-label controlled study. Randomization was performed by flipping a coin by research nurse at the admission of patients if included in the study. The study period was from August 2010 to July 2013. We stop the trial at the end of the study period. Patients who visited the emergency department of the Linkou Chang-Gung Memorial Hospital or the China Medical University Hospital were enrolled. The Linkou Chang Gung Memorial Hospital is a 3000-bed medical center, and the China Medical University Hospital is a medical center that is located in the central area of Taiwan. Patients aged >16 years presenting with evidence of OP poisoning were included in this study. The identification of OP poisoning was based on exposure history, clinical features, and decreased plasma BuChE activity(less than 3000 U/L). The study excluded patients with any of the following conditions: (1) an uncertain history of exposure or an uncertain time of poisoning, (2) carbamate poisoning, (3) coingestion with other fatal intoxicants or fatal injuries, (4) intoxication time more than 24 h, and (5) pregnancy.

### *Treatment protocol*

The patients were randomly divided into a control group and an experimental group. Each enrolled patient was treated with gastric lavage, activated charcoal administration when no contraindications were present and airway protection when needed. Other supportive treatments, such as endotracheal intubation for acute respiratory patients, were also performed when needed. Appropriate atropine doses were administered according to patients' clinical presentations, i.e., 1 mg atropine intravenously every 10 min until “dry lung”. Each enrolled patient was treated with 2 gm PAM intravenously as the loading dose. The control group was treated according to the WHO's recommended PAM regimen, i.e., 500 mg/h. The experimental group was treated according to their APACHE II scores (if that score was ≧26) and dynamic changes in BuChE activity [Fig. 1]. If a patient's APACHE II score was ≧26 or there was no elevation in BuChE activity at the 12th hour when compared to the 6th BuChE activity ($[BuChE]_{12} - [BuChE]_6/[BuChE]_{12}$ <5%), doses of 1 g/h PAM (i.e., doubled WHO's recommended PAM regimen) were given [16,17]. PAM was discontinued when the patient was free of OP poisoning symptoms and signs or the patient experienced treatment failure.