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Prognostic value of plasma C-reactive protein in the evaluation of paraquat poisoning patients

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ABSTRACT

Objective: To investigate the prognostic value of plasma C-reactive protein (CRP) level in patients with paraquat poisoning.
Methods: This study included 162 patients with paraquat poisoning. The data of plasma paraquat, CRP level and arterial blood gas were analyzed. Cox regression analysis was applied to evaluate the risk factors of prognosis. Receiver operating characteristics curve analysis and area under curve were used to calculate the predictive power of significant variable. Differences in patient survival were determined using the Kaplan–Meier method and a log-rank test.
Results: Plasma CRP level was significantly increased in non-survival patients compared with survival patients ($P < 0.05$), and positively correlated with plasma paraquat level ($P < 0.05$). Cox regression analysis revealed that plasma CRP level was an independent prognostic marker of mortality within 30 days. The receiver operating characteristics curve analysis indicated that area under curve of plasma CRP level was 0.867 (95% *CI*: 0.81–0.93), and the cut-off value was 18 mg/L, and patients with CRP level over this value had a poor survival time compared with those with less than this value.
Conclusions: These results suggest that plasma CRP level is distinct increased in patients with paraquat poisoning, and the plasma CRP level may be useful for the prediction of prognosis in paraquat poisoning.

1. Introduction

Paraquat is one of the most widely used potent herbicides in the world, especially in the developing countries, such as China. However, due to its easily accessible, paraquat is frequently ingested by some people, both intentionally and accidentally, and these people often die within a few days. Although distinct advancement has been made in the treatment of paraquat poisoning, the clinical efficacy of these approaches remains indeterminate [1]. A reliable predictor of prognosis of patients with paraquat poisoning may guide treatment and future research. Several prognostic markers have been found to have prognostic significance in the evaluation of patients with paraquat poisoning at present, such as plasma paraquat concentration [2,3], arterial lactate level [4], severity scoring system [5], and arterial blood gas analysis [6]. However, these prognostic markers cannot be applied widely in numerous hospitals in the developing countries, due to the higher requirement of assay or complicated calculation [7].

Several mechanisms have been reported to be involved in the tissue injury caused by paraquat poisoning, such as redox reaction by reactive oxygen species and lipid peroxidation of cellular membranes [8,9]. In addition, inflammatory response is the initial and main mechanism of tissue injury after paraquat poisoning [10]. C-reactive protein (CRP) is an acute-phase protein that has been evaluated extensively in the critical illness [11]. CRP level is positively correlated with the degree of inflammation during the early course of illness [12]. Currently, studies have indicated that CRP is able to predict prognosis and mortality of several

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diseases, such as bacterial infection in cirrhosis [13], H7N9 avian influenza [14] and organophosphate poisoned patients [15]. However, the association of plasma CRP level with the outcome of patients with paraquat poisoning has not been evaluated. Therefore, the aim of the present study was to investigate the potential role of the plasma CRP level as a prognostic marker in patients with paraquat poisoning.

2. Materials and methods

2.1. Patients

This study was carried out in the First Affiliated Hospital of Guangxi Medical University between June 2010 and March 2014. Patients with acute oral paraquat poisoning were enrolled in this study. The duration of follow-up was 30 days. Patients of non-oral ingestion poisoning or paraquat exposure of > 24 h previous to presentation were excluded. We also excluded patients who have inflammatory arthritis and connective tissue disease, malignancies, and recent (< 2 months) surgery or major trauma. All primary data were collected according to procedures outlined in epidemiology guidelines that strengthen the reporting of observational studies. The mortality occurred during the stay at hospital was recorded. The following variables were also collected, including patient's age, gender, admission time, oral paraquat amount. The study protocol was approved by Review Boards Guangxi Medical University for human studies. The requirement for written informed consent was waived because there was no intervention.

2.2. Laboratory analysis

Blood samples were collected immediately following admission. Plasma paraquat was measured quantitatively by high performance liquid chromatography. Arterial blood gas, including PaO_2, $PaCO_2$, HCO_3-, base excess (BE) were determined by blood gas analyzer (GEM premier 3000; Instrumentation Laboratory, Bedford, IL, USA). Liver function variables [alanine transaminase (ALT), aspartate aminotransferase (AST)], renal function [blood urea nitrogen (BUN), creatinine (Cr)] were analyzed by the auto biochemistry analyzer (Automatic Analyzer 7600-120, Hitachi, Tokyo, Japan). CRP level measurements were performed using an immunoturbidimetric method that employed a commercially available test (turbidimetric test, Boehringer Mannheim, Germany).

2.3. Treatment protocol

Patients were given treatment immediately following admission. All the patients were treated under local protocol by gastric lavage, catharsis and fluid diuresis. Briefly, gastric lavage with a large amount of saline was performed every 4 h. Charcoal haemoperfusion with a charcoal-containing (Adsorba, Gambro, Germany) dialysis machine (Surdial, Nipro, Japan) was performed if the urine paraquat value > 5 mg/L. A second session of haemoperfusion was arranged when the urine paraquat value > 5 mg/L at 4 h after the first haemoperfusion administration. Intravenous dexamethasone (20 mg/day) was administrated for another 11 days after methylprednisolone therapy. Cyclophosphamide and methylprednisolone were repeated if the PaO_2 was < 60 mmHg and the duration was > 2 weeks after the initial treatment. Acetylcysteine for injection sodium and Edaravone injection were also administered to the patients.

2.4. Statistical analysis

Data are presented as mean ± SD. Statistically significant differences between the two groups were analyzed using the independent two-sample *t*-test or Mann–Whitney *U* test depending on data distribution. Categorical data were analyzed using the *Chi*-square test. The Pearson correlation test was used for correlation analysis. Cox regression analysis based on forward elimination of data was applied to evaluate the risk factors of prognosis. Receiver operating characteristics (ROC) curve analysis was used to calculate cut-off values, sensitivity, specificity, and overall correctness of designated variable. The best cut-off values were determined by analyzing the Youden's index (sensitivity + specificity−1) and the maximized area under curve (AUC) of the ROC. Kaplan–Meier survival test and log-rank test were used to compare the survival rate between two groups. SPSS statistical software package 16.0 was used to perform statistical analysis. $P < 0.05$ was considered to indicate statistical significance.

3. Results

3.1. Subject characteristics at admission

There were 162 patients with paraquat poisoning enrolled in this study. Among these patients, 75 died and 87 survived after the treatment. We divided these patients into survival group and non-survival group, respectively. The clinical characteristics at admission of the patients are summarized in Table 1. We found that the plasma CRP levels, amount of paraquat intake, ALT, AST, PaO_2, $PaCO_2$, BE, HCO_3-, BUN, Cr, and plasma paraquat level were significantly increased in non-survival group compared with survival group ($P < 0.05$); while age, gender, AST and white blood count had no distinct difference between two groups ($P > 0.05$).

Table 1
Characteristics of 162 paraquat patients at admission.

Parameters	Non-survival (n = 75)	Survival (n = 87)
PPL (μg/mL)	45.17 ± 2.98	25.61 ± 3.02**
Age (years)	29.74 ± 9.50	28.47 ± 10.69
Gender (male/female)	48/27	52/35
Admission time (h)	5.06 ± 1.80	4.44 ± 1.57*
Intake amount (mL)	28.09 ± 1.13	25.89 ± 1.11**
ALT (IU/L)	39.61 ± 5.81	37.80 ± 5.36*
AST (IU/L)	40.51 ± 5.14	39.33 ± 5.50
PaO_2 (mmHg)	7.71 ± 1.07	9.52 ± 0.83**
$PaCO_2$ (mmHg)	5.18 ± 0.44	5.00 ± 0.55*
BE (mmol/L)	4.49 ± 0.28	2.05 ± 0.57**
HCO_3- (mmol/L)	2.25 ± 0.13	2.15 ± 0.09**
BUN (mmol/L)	9.04 ± 0.55	9.21 ± 0.50*
Cr (mmol/L)	99.96 ± 12.00	95.91 ± 11.85*
WBC ($\times 10^9$)	20.55 ± 2.30	19.88 ± 12.25
CRP (mg/L)	23.12 ± 9.14	13.75 ± 6.48**

PPL: Plasma paraquat level; WBC: White blood count. *: $P < 0.05$, **: $P < 0.01$.

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