Kidney Res Clin Pract 35 (2016) 102–106

Kidney Research and Clinical Practice

journal homepage: http://www.krcp-ksn.com
Contents lists available at ScienceDirect

Original Article

Predicting the probability of survival in acute paraquat poisoning☆

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Article history:
Received 1 October 2015
Received in revised form
24 January 2016
Accepted 31 January 2016
Available online 27 February 2016

Keywords:
Creatinine
Logistic models
Paraquat
Prognosis

Abstract

Background: Paraquat (PQ) concentration–time data have been used to predict prognosis for 3 decades. The aim of this study was to find a more accurate method to predict the probability of survival.

Methods: This study included 788 patients with PQ poisoning who were diagnosed using plasma PQ concentration between January 2005 and August 2012. We divided these patients into 2 groups (survivors vs. nonsurvivors), compared their clinical characteristics, and analyzed the predictors of survival.

Results: The mean age of the included patients was 57 years (range, 14–95 years). When we compared clinical characteristics between survivors (n = 149, 19%) and nonsurvivors (n = 639, 81%), survivors were younger (47 ± 14 years vs. 59 ± 16 years) and had lower plasma PQ concentrations (1.44 ± 8.77 μg/mL vs. 80.33 ± 123.15 μg/mL) than nonsurvivors. On admission, serum creatinine was lower in survivors than in nonsurvivors (0.95 ± 0.91 mg/dL vs. 1.88 ± 1.27 mg/dL). In multivariate logistic regression analysis, age and logarithmically converted serum creatinine [ln(Cr)], [ln(time)], and [ln(PQ)] were assessed as prognostic factors to predict survival in PQ poisoning. The predicted probability of survival using significant prognostic factors was exp (logit)/[1 + exp(logit)], where logit = −1.347 + [0.212 × sex (male = 1, female = 0)] + (0.032 × age) + [1.551 × ln(Cr)] + [0.391 × ln(hours since ingestion)] + [1.076 × ln(plasma PQ μg/mL)]. With this equation, the sensitivity and specificity were 86.5% and 98.7%, respectively.

Conclusion: Age, ln(Cr), ln(time), and ln(PQ) were important prognostic factors in PQ poisoning, and our equation can be helpful to predict the survival in acute PQ poisoning patients.

Introduction

Paraquat (PQ; 1,1'-dimethyl-4,4'-bipyridinium) dichloride is a nonselective herbicide that has been widely used in many countries since the 1960s. It has unique properties which make it important to agriculture; it is a fast-acting broad-spectrum contact weedkiller which is very rainfast and is deactivated on contact with soil. However, ingestion of the concentrated formulation is very toxic to humans with no specific antidote or

☆ The authors alone were responsible for the content and writing of the paper.

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http://dx.doi.org/10.1016/j.krcp.2016.01.003

conclusively effective treatment demonstrated [1]. PQ has been used for the past 3 decades in Korea, with an estimated 2,000 toxic ingestions annually [2]. Because there are few effective treatments for the management of PQ poisoning, it is important to predict patient mortality. Early prediction of inevitable death would allow the cessation of inappropriate treatments in acute PQ poisoning [3].

The prognosis of acute PQ poisoning is dependent on the plasma PQ concentrations, and PQ concentration−time data have been used to predict outcomes for 3 decades [4]. Because a nomogram was introduced to relate the patient outcome to the plasma PQ level and the time from poisoning to blood sampling, other graphs and formulas have been reported [5−9]. However, these studies involved small sample sizes and were better at predicting death than survival [10]. Recently, biomarkers such as pentraxin-3 or neutrophil gelatinase−associated lipocalin were used to predict the prognosis in patients with PQ poisoning [11,12].

Therefore, we investigated prognostic factors affecting survival in patients with PQ poisoning and estimated the predicted probability of survival through logistic regression analysis using plasma PQ concentration, time since ingestion, and other variables.

Methods

Patient selection

Eight hundred ten patients who had ingested PQ visited our hospital between January 2005 and December 2012. We excluded 22 patients who were transferred to other hospitals during treatment or otherwise lost to follow-up. Therefore, 788 patients were included in this study and were divided into 2 groups: survival ($n = 149$) and nonsurvival ($n = 639$). Patients who lived for more than 3 months were included in the survival group. This study was approved by the Institutional Review Board of Presbyterian Medical Center.

Data collection and study variables

Physicians treated the patients and recorded all the information on a standardized data collection form. Standardized medical emergency procedures were conducted according to the Presbyterian Medical Center protocol for PQ poisoning (Table 1). Briefly, gastric lavage was performed, and 100 g of Fuller's earth in 200 mL of 20% mannitol was given if poisoning had occurred within the previous 12 hours. Hemoperfusion was performed if a urinary PQ test was positive within 24 hours. Urinary PQ was checked semiquantitatively with the dithionite method on arrival [13]. These results were presented as Grades 1–4, where black = + 4, deep blue = + 3, light blue = + 2, and barely distinguishable blue = + 1.

We developed 3 models to predict survival according to the interval after ingestion and initial creatinine. Model 1 was based on the initial plasma PQ concentration and time since ingestion. Model 2 was based on adding of prognostic factors to predict the survival of the patients with PQ poisoning in our study to Model 1. Model 3 was based on a 2-hour PQ level instead of the initial PQ level.

Table 1. Summary of treatment guidelines for acute paraquat intoxication

1. Gastric lavage
2. Dithionite urine test
3. Fuller's earth, 100 g in 200-mL mannitol
4. A. Antioxidant (intravenous administration)
Vitamin B and E
B. For renal preservation
Furosemide
15% mannitol
5. Emergency hemoperfusion
6. Key laboratory parameters
Blood chemistry: blood urea nitrogen, creatinine, amylase, lipase
Electrolyte: Na, K, Cl
Arterial blood gas analysis
Plasma paraquat level

Examination of plasma PQ concentration

Blood samples for the measurement of plasma PQ concentration (PQ 0 hour) were collected as soon as patients arrived at the emergency department. Samples were centrifuged at 1,600 × *g* for 15 minutes at 4°C and analyzed at the Christian Medical Research Center. If patients arrived within 4 hours of ingestion, another blood sample (PQ 2 hours) was collected 2 hours later. PQ levels were measured using high-performance liquid chromatography.

Statistical analysis

All data are presented as mean ± standard deviation unless otherwise specified. Differences in covariates between survivors and nonsurvivors were tested with the Student *t* test for continuous variables and the chi-square test for categorical variables. Multiple logistic regression analysis was applied to predict the outcome after acute PQ poisoning. In this study, time since ingestion (in hours), serum creatinine, and plasma PQ level were used in multiple logistic regression analysis after logarithmic conversion as they did not display a normal distribution. To determine the sensitivity and specificity of the prediction equation, receiver operating characteristic curves were generated. A P value of < 0.05 was considered statistically significant. Statistical analysis was carried out using SPSS software, version 21 (IBM corporation, New York, NY, USA) and MedCalc 12.5 (MedCalc Software bvba, Mariakerke, Belgium).

Table 2. Clinical and laboratory findings of the 788 patients with PQ poisoning

Characteristics	
Age (y)	57 ± 16
Male	507 (64)
Time since ingestion (h)	6.6 ± 15.0
Hemoperfusion therapy	594 (75)
Serum creatinine (mg/dL)	1.7 ± 1.3
Serum alanine aminotransferase (IU/L)	36 ± 50
Serum lipase (IU/L)	103 ± 184
P_{CO_2} (mmHg)	25.0 ± 9.1
HCO_3 (mmol/L)	14.8 ± 6.8
Amount of PQ ingested (mL)	151 ± 124
Plasma PQ 0-h level (μg/mL)	65 ± 115
Plasma PQ 2-h level (μg/mL)*	41 ± 80
Urine PQ test	
Negative	30 (3.8)
Weakly positive	84 (10.6)
Positive	44 (5.6)
Strong positive	632 (80)

Data are presented as mean ± SD or number (%).
* The data are available in 379 patients.
PQ, paraquat.