Clinical Research Report

Journal of INTERNATIONAL MEDICAL RESEARCH

Journal of International Medical Research
2019, Vol. 47(9) 4194–4203

DOI: 10.1177/0300060519860032
journals.sagepub.com/home/imr
SAGE

Clinical features and risk factors of acute kidney injury in children with acute paraquat intoxication

Yue Song[1,2], Chaofeng Li[1], Fenglan Luo[1] and Yuhong Tao[1]

Abstract

Objective: This study aimed to investigate the clinical features and risk factors of acute kidney injury (AKI) in children with acute paraquat intoxication.

Methods: A retrospective study of 110 hospitalized children with acute paraquat intoxication in West China Second University Hospital, Sichuan University was conducted from January 2010 to May 2017. The Kaplan–Meier method was used to compare the survival rates of children with different AKI stages. Multivariate logistic regression was applied to analyse the risk factors for paraquat-induced AKI.

Results: AKI occurred in 42 of 110 (38.2%) children. We observed AKI stage 1 in two (4.8%) children, AKI stage 2 in 11 (26.2%), and AKI stage 3 in 29 (69.0%). The survival rate of children in AKI stage 3 (34.5%) was significantly lower than that in children in AKI stage 2 (63.6%) and AKI stage 1 (100%). Multivariate analysis showed that oral ulcers and elevated blood glucose levels were significant independent risk factors for paraquat-induced AKI in children (odds ratio = 4.223 and 5.545, respectively).

Conclusions: The incidence and mortality rates of paraquat-induced AKI in children are high. Oral ulcers and elevated blood glucose levels are independent risk factors affecting the occurrence of paraquat-induced AKI in children.

Keywords

Paraquat, intoxication, children, acute kidney injury, risk factor, oral ulcer, glucose

Date received: 31 January 2019; accepted: 6 June 2019

[1]Department of Pediatrics, West China Second University Hospital, Sichuan University, Chengdu, China
[2]Key Laboratory of Birth Defects and Related Diseases of Women and Children (Sichuan University), Ministry of Education, Chengdu, China

Corresponding author:
Yuhong Tao, Department of Pediatrics, West China Second University Hospital, Sichuan University, No. 20, Section 3, Renmin Nan Lu, Chengdu 610041, China.
Email: hxtyh@sina.com

Introduction

Paraquat is a non-selective cationic herbicide. By blocking photosynthesis-related reduction of oxidized coenzyme II ($NADP^+$) into reduced coenzyme II (NADPH) in plant cells, paraquat leads to accumulation of reactive oxygen species and cell death, thus achieving rapid weeding.[1]Paraquat has a highly toxic effect on humans, and its minimum lethal dose is 30 mg/kg. There is no specific antidote for acute paraquat intoxication and its mortality rate is high.[2]

Paraquat affects multiple organ systems throughout the body and can lead to multiple organ dysfunction syndrome in severe cases. According to the toxicokinetic process of paraquat,[1] the kidney is also a main target organ after poisoning. A total of 90% of paraquat is excreted from the kidney in its original form within 12 to 24 hours.[3] The mechanisms of paraquat-induced acute kidney injury (AKI) include oxidative stress, inflammatory response, apoptosis, and renal haemodynamic changes.[4–9] Some clinical studies have also indicated that paraquat-induced AKI precedes acute lung injury,[10] peaks within the next 3 to 5 days, and then returns to normal renal function in some patients within 3 weeks.[11] Ecker et al.[12] also found that paraquat removal from the kidney is biphasic, including rapid and slow clearance stages. AKI further reduces the clearance rate of paraquat, increases accumulation of paraquat in lung tissue, and promotes pulmonary interstitial fibrosis. Therefore, early prevention and treatment of AKI is important for reducing the mortality of acute paraquat intoxication. However, current research on paraquat-induced AKI has mainly focussed on adult patients and has paid less attention to children.[11] Therefore, the current study aimed to retrospectively analyse clinical features and risk factors of paraquat-induced AKI in children.

Methods

Patients

This research was approved by the Ethics Committee of West China Second University Hospital, Sichuan University. Informed consent was obtained from the children's guardians. Children with acute paraquat intoxication who were hospitalized in West China Second University Hospital, Sichuan University from January 2010 to May 2017 were enrolled.

Acute paraquat intoxication was diagnosed if one of the following conditions was met: (1) the patient or his/her family members provided a history of taking paraquat; (2) for those who did not admit to taking paraquat, but additional evidence was found, including an empty paraquat bottle, black-green residue on the skin, vomiting of unknown causes, oral mucosal erosion, or ulcers; and (3) paraquat was positive in blood or urine. Exclusion criteria were as follows: (1) a history of serious chronic diseases, such as heart, liver, kidney, and lung diseases; and (2) paraquat intoxication combined with other drug poisoning. The AKI diagnostic and staging criteria proposed by the Kidney Disease Improving Global Outcomes (KDIGO) 2012 guidelines were adopted.[13]

Treatment

Immediately after admission, a blood count, liver function, renal function, blood glucose levels, electrolytes, and coagulation function were measured, and a chest computed tomography (CT) examination was performed. Routine treatment before and after admission included vomiting induction, gastric lavage, oral activated carbon, catharsis to prevent absorption of toxic substances, and diuresis to promote excretion of toxic substances. The patients were administered 15 mg/kg/day

methylprednisolone. Within 1 to 3 days after poisoning, haemoperfusion was administered for 2 hours, once a day, three to five times, until paraquat could not be detected in the blood. For patients with multiple organ dysfunction, haemodialysis or continuous renal replacement therapy was used. Patients with respiratory failure were provided continuous low-flow oxygen inhalation or mechanical ventilation.

Data collection

Data of age, sex, cause of intoxication, time from intoxication to treatment, time from intoxication to blood purification, main clinical manifestations and laboratory results, paediatric critical illness score (PCIS), clinical type of acute paraquat intoxication, and prognosis were collected. All children were followed up by telephone for at least 3 months.

The PCIS includes 11 items as follows:[14] heart rate, blood pressure, respiration rate, arterial partial pressure of oxygen, pH value, serum sodium, serum potassium, urea nitrogen, serum creatinine, haemoglobin, and gastrointestinal symptoms (stress ulcer bleeding or intestinal paralysis). The lower the score is, the more serious the condition is. A score of >80 is non-critical, 71–80 is critical, and <70 is extremely critical.

The clinical type of acute paraquat intoxication can be categorized as follows. (1) The mild type is defined as minimal intake. Except for skin and oral mucosa damage, there are no digestive tract symptoms, such as nausea, vomiting, and diarrhoea, and no liver, kidney, heart, pancreas, lung, and other organ function damage, and the progress is slow. (2) The moderate type is defined as moderate intake with moderate organ dysfunction, such as gastrointestinal bleeding, abnormal liver function, AKI, acute lung injury, and acute pancreatitis. (3) The severe type is defined as high intake, with obvious organ dysfunction or more than three organs involved, rapid progress, and most children die within hours to days.

Statistical analysis

All the data were analysed using IBM SPSS Statistics Version 20 (IBM Corp., Armonk, NY, USA). Normally distributed data are presented as the mean ± standard deviation. Data with a skewed distribution are expressed as the median (quartile). Continuous variables were analysed using the Student's *t*-test. The Mann–Whitney *U* test was used for non-normally distributed data. Kaplan–Meier survival analysis was used to analyse the survival rate of children with AKI. Logistic regression analysis was used for correlation analysis. The results were considered significant when $P < 0.05$.

Results

Demographic characteristics

A total of 110 children suffered from acute paraquat intoxication. Among these children, 38 were younger than 6 years (34.6%) and 72 were older than 6 years (65.4%). The majority of children younger than 6 years were boys (60.5%). All of the poisoning causes were accidental. Girls were the majority (61.1%) among children older than 6 years. The causes of poisoning were accidental ingestion (63.9%) and suicide (36.11%) (Table 2).

Clinical features of AKI induced by acute paraquat intoxication

AKI was found in 42 of 110 (38.2%) children. Among these children, we observed AKI stage 1 in two (4.8%) children, AKI stage 2 in 11 (26.2%), and AKI stage 3 in 29 (69.0%). Of the 110 children analysed, 26 (23.6%) died. Among the deceased

Table 1. Demographic characteristics of 110 children with acute paraquat intoxication.

				Sex		Cause of intoxication	
Age (years)	n (%)	AKI, n (%)	Death, n (%)	Male, n (%)	Female, n (%)	Accidental, n (%)	Suicide, n (%)
Approximately 3	23 (20.9)	1 (2.4)	0	12 (52.2)	11 (47.8)	23 (100)	0
Approximately 6	15 (13.6)	3 (7.1)	3 (11.5)	11 (73.3)	4 (26.7)	15 (100)	0
Approximately 12	32 (29.1)	14 (33.3)	9 (34.6)	14 (43.8)	18 (56.2)	23 (71.9)	9 (28.1)
>12 years	40 (36.4)	24 (57.2)	14 (53.9)	14 (35.0)	26 (65.0)	23 (57.5)	17 (42.5)
Total	110	42	26	51	59	84	26

AKI: acute kidney injury.

children, significantly more children died in the AKI group (n = 23, 54.8%) than in the non-AKI group (n = 3, 4.4%) ($P < 0.001$). Among the children who died, all children died within 2 weeks, 10 (37.0%) died within 3 days, and two (7.4%) died on the day of admission. Among AKI cases, all children in AKI stage 1 survived, four (36.4%) in AKI stage 2 died, and 19 (65.5%) in AKI stage 3 died. Figure 1 shows that the survival rate of children in AKI stage 3 was significantly lower than that of children in AKI stages 2 and 1 ($P < 0.05$).

Children in the AKI group were mainly older than 6 years, with a significant difference in age distribution compared with the non-AKI group ($P < 0.001$). There was no significant difference in sex distribution or poisoning causes between the AKI and non-AKI groups. Among the 110 children, the time from intoxication to consultation was within 6 hours in 12 (10.9%), 6–24 hours in 53 (48.2%), and over 24 hours in 45 (49.9%) children. Blood purification was performed in 84 children. Of these 84 children, 51 (69.7%) received haemoperfusion, six (7.14%) received haemoperfusion and haemodialysis, 25 (29.8%) received haemoperfusion and plasma exchange, and two (2.4%) received continuous venovenous haemofiltration. The time from intoxication to blood purification was within 6 hours in five (6.0%) children, 6 to 24 hours in 37 (44.0%), and more than 24 hours in 42 (50.0%). However, there were no significant differences in the time from intoxication to consultation and the time from intoxication to blood purification between the AKI and non-AKI groups. The rates of vomiting, abdominal pain, and oral ulcers were higher, and the blood count, percentage of neutrophils, and levels of alanine aminotransferase, aspartate aminotransferase, total bilirubin, serum sodium, serum potassium, and lactate dehydrogenase were higher in the AKI group compared with the non-AKI group (all $P < 0.01$). The clinical type of acute paraquat intoxication in the AKI group was significantly more severe than that in the non-AKI group ($P < 0.001$). The PCIS was significantly lower in the AKI group than in the non-AKI group ($P < 0.001$). There was no significant difference in gastrointestinal bleeding, platelet count, or albumin levels between the AKI and non-AKI groups (Table 2).

Risk factors for AKI induced by acute paraquat intoxication

First, all possible risk factors that affected AKI induced by acute paraquat intoxication were included in a logistic regression

Table 2. Clinical characteristics of 110 children with acute paraquat intoxication.

Variable	AKI (n = 42)	Non-AKI (n = 68)	*P* value
Age (years)			<0.001
Approximately 3	1 (2.4)	22 (32.4)	
Approximately 6	3 (7.1)	12 (17.6)	
Approximately 12	14 (33.3)	14 (20.6)	
> 12	24 (57.2)	20 (29.4)	
Sex (n)			0.172
Male	16 (38.1)	35 (51.5)	
Female	26 (61.9)	33 (48.5)	
Cause of intoxication (n)			0.172
Accidental	29 (69.0)	55 (80.9)	
Suicide	13 (31.0)	13 (19.1)	
Time from intoxication to consultation (hours)			0.207
Approximately 6	7 (16.7)	5 (7.4)	
Approximately 24	20 (47.6)	33 (48.5)	
>24	15 (35.7)	30 (44.1)	
Time from intoxication to blood purification (hours)			0.363
Approximately 6	4 (10.0)	1 (2.3)	
Approximately 24	20 (50.0)	17 (38.6)	
>24	16 (40.0)	26 (59.1)	
PCIS (points)	82.70 ± 9.03	96.09 ± 3.96	<0.001
Clinical type			<0.001
Mild	2 (4.8)	44 (64.7)	
Moderate	14 (33.3)	22 (32.4)	
Severe	26 (61.9)	2 (2.9)	
Main manifestation (n)			
Vomiting	27 (64.3)	21 (30.9)	0.001
Abdominal pain	16 (38.1)	7 (10.3)	0.002
Oral ulcer	26 (61.9)	22 (32.4)	<0.001
Gastrointestinal bleeding	6 (14.3)	2 (2.9)	0.052
Main laboratory test			
Peripheral white blood cells ($\times 10^9$/L)	14.66 ± 6.89	10.83 ± 4.01	<0.001
Platelet count ($\times 10^9$/L)	270.03 ± 102.42	242.20 ± 87.70	0.192
Neutrophil ratio (%)	83.43 ± 11.97	65.03 ± 19.46	<0.001
Alanine aminotransferase(M [$P_{25,}$ P_{75}], U/L)	49 (30, 314.5)	35 (26, 42.5)	0.001
Aspartate aminotransferase (M [P_{25}, P_{75}], U/L)	57 (27, 178.5)	30 (20, 41)	0.001
Total bilirubin (M [P_{25}, P_{75}], U/L)	15.8 (7.35, 48.1)	8.2 (6.0, 12.6)	<0.001
Direct bilirubin (M [P_{25}, P_{75}], U/L)	0 (0, 28.4)	0 (0, 0)	<0.001
Albumin (M [P_{25}, P_{75}], g/L)	41.4 (35.6, 45.8)	44.5 (42.3, 47.6)	0.137
Lactate dehydrogenase (U/L)	865.52 ± 652.62	597.10 ± 165.55	0.002
Serum sodium (mmol/L)	137.98 ± 3.65	133.49 ± 6.61	<0.001
Serum potassium (mmol/L)	3.85 ± 0.48	3.49 ± 0.71	0.002
Blood sugar (mmol/L)	7.03 ± 1.85	6.22 ± 3.23	0.029
Haematuria (n)	5 (11.9)	4 (5.9)	0.298
Proteinuria (n)	20 (47.6)	12 (17.6)	<0.001

Values are mean ± standard deviation, n (%), or M (P_{25}, P_{75}). AKI: acute kidney injury; PCIS: paediatric critical illness score; M (P_{25}, P_{75}): median (25th percentile, 75th percentile).

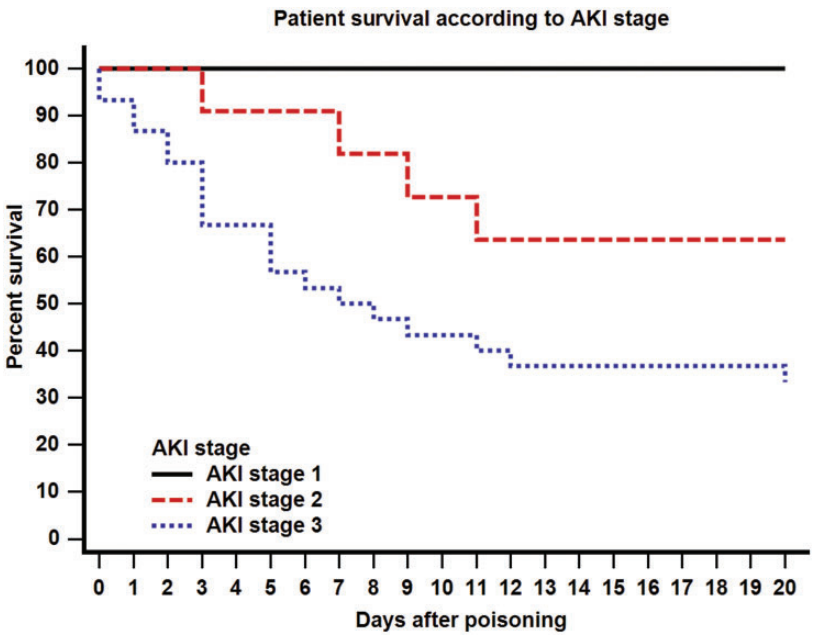

Figure 1. Survival curve of acute kidney injury in children with acute paraquat intoxication

model. Second, the variables with $P < 0.05$ in univariate analysis, as well as the time from intoxication to medical treatment and the time from intoxication to blood purification, were included in the multivariate regression model for regression analysis. Finally, multivariate stepwise regression analysis was conducted to examine the risk factors for AKI induced by acute paraquat intoxication.

Table 3 shows that age > 6 years old, vomiting, abdominal pain, gastrointestinal bleeding, oral ulcers, hypoproteinaemia, increased total white blood cells, increased percentage of neutrophils, hyponatraemia, hypokalaemia, and elevated glutamic-pyruvic aminotransferase levels were risk factors for AKI in children with acute paraquat intoxication (all $P < 0.05$). Further multivariate regression analysis showed that oral ulcers and elevated blood glucose levels were independent risk factors for AKI in children with acute paraquat intoxication (both $P < 0.05$).

Discussion

The degree of renal damage caused by acute paraquat intoxication greatly varies. The main pathological manifestations of acute paraquat intoxication are acute tubular necrosis and ischaemic glomerulopathy. Mild cases may manifest as simple urinary abnormalities, such as proteinuria and/or haematuria. However, severe cases may manifest as acute renal failure and even require renal replacement therapy.[11] The prognosis of AKI with acute paraquat intoxication is poor. In previous studies from adult patients, the incidence and mortality of paraquat-induced AKI were 46.4% to 85.4% and 35.4% to 78.3%, respectively.[11,15–23] In the present study, the incidence and mortality rates of AKI were 38.2% and 23.6%, respectively, which are lower than those reported previously in adults. The causes for this difference may be as follows: (1) the present group of patients were children, among

Table 3. Risk factors for acute kidney injury in 110 children with acute paraquat intoxication.

Variable	B	SE	OR (95% CI)	*P* value
Univariate analysis				
Age (>6 years)	2.134	0.579	8.444 (2.714–26.272)	<0.001
Female	0.544	0.400	1.723 (0.787–3.773)	0.173
Suicide	0.064	0.454	1.897 (0.778–4.621)	0.159
Vomiting	1.393	0.415	4.029 (1.785–9.095)	0.001
Abdominal pain	1.679	0.510	5.363 (1.973–14.574)	0.001
Oral ulcer	1.223	0.410	3.398 (1.521–7.590)	0.003
Gastrointestinal bleeding	1.705	0.842	5.500 (1.055–28.668)	0.043
Increased white blood cell count	0.928	0.403	2.259 (1.149–5.568)	0.021
Increased proportion of neutrophils	2.130	0.639	8.412 (2.402–29.456)	0.001
Hyponatraemia	3.169	1.067	23.774 (2.938–192.389)	0.003
Hypokalaemia	1.567	0.462	4.971 (1.938–11.847)	0.001
Elevated blood sugar	1.705	0.441	5.504 (2.319–13.064)	<0.001
Elevated direct bilirubin	2.048	0.529	7.750 (2.747–21.864)	<0.001
Hypoproteinaemia	1.478	0.431	4.385 (1.884–10.203)	0.001
Elevated alanine aminotransferase	3.209	0.783	24.750 (5.339–114.730)	<0.001
Elevated aspartate transaminase	2.167	0.547	13.696 (4.687–40.022)	<0.001
Elevated lactate dehydrogenase	0.548	0.396	1.729 (0.796–3.758)	0.167
Elevated total bilirubin	2.690	0.669	14.733 (3.971–54.669)	<0.001
Time from intoxication to blood purification (>24 hours)	−0.826	0.449	0.438 (0.182–1.057)	0.066
Time from intoxication to consultation (>24 hours)	−0.351	0.404	0.704 (0.319–1.554)	0.385
PCIS (>80 points)	−2.246	0.560	0.106 (0.035–0.317)	<0.001
Clinical type (moderate to severe)	2.857	0.584	17.417 (5.548–56.678)	<0.001
Multifactor analysis				
Oral ulcer	1.441	0.713	4.223 (1.045–17.068)	0.043
Elevated blood glucose	1.713	0.731	5.545 (1.323–23.241)	0.019
Elevated total bilirubin	1.757	0.907	5.793 (0.979–32.271)	0.053

Increased white blood cell count ($>1.2 \times 10^9$/L); increased neutrophils (< 1 year: 5.85%–48.57%; 1–6 years: 21.9%–68.5%; 7–12 years: 23.6%–75%; ≥13 years: 50%–70%); elevated alanine aminotransferase levels (>72 U/L); elevated aspartate aminotransferase levels (>59 U/L); elevated total bilirubin levels (>22 μmol/L); hypoproteinaemia (<35 g/L); elevated lactate dehydrogenase levels (>618 U/L); hyponatraemia (<130 mmol/L); hypokalaemia (<3.5 mmol/L); elevated blood glucose levels (≥6.0 mmol/L); and elevated direct bilirubin levels (>0 μmol/L). SE: standard error; OR: odds ratio; CI: confidence interval; PCIS: paediatric critical illness score.

whom mistaking paraquat was the main cause of intoxication, which means less ingestion; and (2) active blood purification, such as haemoperfusion, was conducted to remove paraquat from the blood. Additionally, the present study showed that the AKI group had more severe clinical manifestations, a lower PCIS, and higher mortality rate compared with the non-AKI group. Therefore, AKI staging is an important index to evaluate the severity of children with acute paraquat intoxication.

The outcomes are directly related to the severity of AKI.[24] A slight increase in serum creatinine levels can lead to an increase in complications and mortality. A 26.5-μmol/L increase in serum creatinine levels can increase the mortality 4.1 times.[25] The present study showed that the survival rate of AKI stage 3 was significantly lower

than that of AKI stages 2 and 1. This finding suggests that AKI staging can be used as a simple and practical tool to assess the severity and prognosis of acute paraquat intoxication in children. The prognosis of paraquat-induced AKI is closely related to the severity of AKI. AKI staging is a risk factor for a poor prognosis of acute paraquat intoxication.

The occurrence of AKI in acute paraquat intoxication is affected by many factors. The present study showed that oral ulcers and hyperglycaemia were independent risk factors for paraquat-induced AKI. Oral paraquat poisoning has a burning sensation, resulting in oral and oesophageal mucosal erosion ulcers.[25] Oral ulcers can be used as prognostic factors for early evaluation of oral paraquat poisoning.[26] The more serious the oral ulcer is, the more serious the disease is. Once oral ulcers occur, paraquat poisoning is more serious. For children with acute paraquat intoxication with oral ulcers, physicians need to be aware of the occurrence of AKI. Paraquat can also activate the locus coeruleus–sympathetic–adrenal medullary system, inhibit insulin secretion, stimulate glucagon secretion, cause insulin resistance, accelerate glycogen decomposition, strengthen gluconeogenesis, and lead to acute elevation of blood glucose levels. Previous studies have suggested that hyperglycaemia is a risk factor for pulmonary fibrosis in acute paraquat intoxication.[27] Furthermore, blood glucose levels can predict the prognosis of paraquat intoxication.[27,28] As mentioned above, the present study suggested that increased blood glucose levels were an independent risk factor for AKI in acute paraquat intoxication. Therefore, for children with acute paraquat intoxication, blood glucose should be monitored and hyperglycaemia should be controlled. Previous adult studies have suggested that the time from intoxication to medical treatment and the time from intoxication to blood purification are risk factors for AKI in acute paraquat intoxication.[11,23] However, the present study showed that there were no significant differences in the time from intoxication to treatment and the time from intoxication to blood purification between the AKI and non-AKI groups. This finding is consistent with the finding of Liu et al.[27] and Fengjun et al.[29] We believe that the time from intoxication to consultation and the time from intoxication to blood purification are usually inaccurate and may be affected by many factors in clinical practice, especially for children. Additionally, the dosage of paraquat is an important factor affecting the prognosis of patients. However, most of the children suffered from accidental ingestion or suicide. Clinicians have difficulty accurately estimating the dose of paraquat.

This was a retrospective study and there are some limitations as follows. (1) Blood or urine paraquat detection cannot be widely carried out in most hospitals in China. Therefore, the relationship between paraquat concentrations in blood and AKI was not analysed. (2) The present study only detected serum urea nitrogen and creatinine levels, but neutrophil gelatinase-related apolipoprotein and other early damage biomarkers of AKI were not tested.[16,30] (3) Clinicians had difficulty in accurately estimating the dose of paraquat because most of the children suffered from accidental ingestion or suicide. Therefore, the dose of paraquat was not included in prognostic factor analysis.

In conclusion, the incidence of paraquat-induced AKI and its mortality are high, and the outcomes are directly related to the severity of paraquat-induced AKI in children. Physicians should be aware of AKI in children with acute paraquat intoxication. Oral ulcers and elevated blood glucose levels are independent risk factors for AKI in children with acute paraquat

intoxication. For high-risk patients with AKI, close monitoring and timely intervention are required.

Declaration of conflicting interest

The authors declare that there is no conflict of interest.

Funding

The authors received financial support for the research of this article from the foundation of the Science & Technology Department of Sichuan Province (No. 2017JY0016).

ORCID iD

Yuhong Tao https://orcid.org/0000-0001-8074-4170

References

1. Dinis-Oliveira RJ, Duarte JA, Sánchez-Navarro A, et al. Paraquat poisonings: mechanisms of lung toxicity, clinical features, and treatment. *Crit Rev Toxicol* 2008; 38: 13–71.
2. Yoon SC. Clinical outcome of paraquat poisoning. *Korean J Intern Med* 2009; 24: 93–94.
3. Magalhães N, Carvalho F and Dinis-Oliveira RJ. Human and experimental toxicology of diquat poisoning: toxicokinetics, mechanisms of toxicity, clinical features, and treatment. *Hum Exp Toxicol* 2018; 37: 1131–1160.
4. Park EK, Mak SK, Kültz D, et al. Determination of cytotoxicity of nephrotoxins on murine and human kidney cell lines. *J Environ Sci Health B* 2008; 43: 71–74.
5. Awadalla EA. Efficacy of vitamin C against liver and kidney damage induced by paraquat toxicity. *Exp Toxicol Pathol* 2012; 64: 431–434.
6. Salazar-Lugo R, Mata C, Oliveros A, et al. Histopathological changes in gill, liver and kidney of neotropical fish Colossoma macropomum exposed to paraquat at different temperatures. *Environ Toxicol Pharmacol* 2011; 31: 490–495.
7. Machaalani R, Lazzaro V and Duggin GG. The characterisation and uptake of paraquat in cultured baboon kidney proximal tubule cells (bPTC). *Hum Exp Toxicol* 2001; 20: 90–99.
8. Fujimoto Y, Yokota M, Ohdate Y, et al. Effects of Fe2+, Fe3+ and desferrioxamine on paraquat accumulation by rabbit kidney cortex slices. *Res Commun Chem Pathol Pharmacol* 1991; 73: 115–118.
9. Nagao M, Takatori T, Inoue K, et al. Immunohistochemical localization and dynamics of paraquat in small intestine, liver and kidney. *Toxicology* 1990; 63: 167–182.
10. Pavan M. Acute kidney injury following Paraquat poisoning in India. *Iran J Kidney Dis* 2013; 7: 64–66.
11. Kim SJ, Gil HW, Yang JO, et al. The clinical features of acute kidney injury in patients with acute paraquat intoxication. *Nephrol Dial Transplant* 2009; 24: 1226–1232.
12. Ecker JL, Hook JB and Gibson JE. Nephrotoxicity of paraquat in mice. *Toxicol Appl Pharmacol* 1975; 34: 178–186.
13. Palevsky PM, Liu KD, Brophy PD, et al. KDOQI US commentary on the 2012 KDIGO clinical practice guideline for acute kidney injury. *Am J Kidney Dis* 2013; 61: 649–672.
14. Zhang L, Huang H, Cheng Y, et al. Predictive value of four pediatric scores of critical illness and mortality on evaluating mortality risk in pediatric critical patients. *Zhonghua Wei Zhong Bing Ji Jiu Yi Xue* 2018; 30: 51–56.
15. Suntres ZE. Role of antioxidants in paraquat toxicity. *Toxicology* 2002; 180: 65–77.
16. Mohamed F, Buckley NA, Jayamanne S, et al. Kidney damage biomarkers detect acute kidney injury but only functional markers predict mortality after paraquat ingestion. *Toxicol Lett* 2015; 237: 140–150.
17. Mohamed F, Endre Z, Jayamanne S, et al. Mechanisms underlying early rapid increases in creatinine in paraquat poisoning. *PLoS One* 2015; 10: e0122357.
18. Kim JH, Gil HW, Yang JO, et al. Serum uric acid level as a marker for mortality and acute kidney injury in patients with

acute paraquat intoxication. *Nephrol Dial Transplant* 2011; 26: 1846–1852.
19. Seok S, Kim YH, Gil HW, et al. The time between paraquat ingestion and a negative dithionite urine test in an independent risk factor for death and organ failure in acute paraquat intoxication. *J Korean Med Sci* 2012; 27: 993–998.
20. Moon JM and Chun BJ. The efficacy of high doses of vitamin C in patients with paraquat poisoning. *Hum Exp Toxicol* 2011; 30: 844–850.
21. Gil HW, Yang JO, Lee EY, et al. Clinical implication of urinary neutrophil gelatinase-associated lipocalin and kidney injury molecule-1 in patients with acute paraquat intoxication. *Clin Toxicol (Phila)* 2009; 47: 870–875.
22. Koo JR, Kim JC, Yoon JW, et al. Failure of continuous venovenous hemofiltration to prevent death in paraquat poisoning. *Am J Kidney Dis* 2002; 39: 55–59.
23. Weng CH, Chen HH, Hu CC, et al. Predictors of acute kidney injury after paraquat intoxication. *Oncotarget* 2017; 8: 51345–51354.
24. Chertow GM, Burdick E, Honour M, et al. Acute kidney injury, mortality, length of stay, and costs in hospitalized patients. *J Am Soc Nephrol* 2005; 16: 3365–3370.
25. Yang CJ, Lin JL, Lin-Tan DT, et al. Spectrum of toxic hepatitis following intentional paraquat ingestion: analysis of 187 cases. *Liver Int* 2012; 32: 1400–1406.
26. Hong SY, Yang DH and Hwang KY. Associations between laboratory parameters and outcome of paraquat poisoning. *Toxicol Lett* 2000; 118: 53–59.
27. Liu Z, Ji H, Wang H, et al. The prognostic value of the Acute Kidney Injury Network criteria in patients with acute paraquat poisoning. *Zhonghua Wei Zhong Bing Ji Jiu Yi Xue* 2014; 26: 223–227.
28. Huang NC, Hung YM, Lin SL, et al. Further evidence of the usefulness of Acute Physiology and Chronic Health Evaluation II scoring system in acute paraquat poisoning. *Clin Toxicol (Phila)* 2006; 44: 99–102.
29. Fengjun J, Wen Z, Taoning W, et al. Analysis of risk factors for prognosis of patients with acute paraquat intoxication. *Zhonghua Wei Zhong Bing Ji Jiu Yi Xue* 2015; 27: 906–910.
30. Roberts DM, Wilks MF, Roberts MS, et al. Changes in the concentrations of creatinine, cystatin C and NGAL in patients with acute paraquat self-poisoning. *Toxicol Lett* 2011; 202: 69–74.