Fatality in paraquat poisoning

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ABSTRACT

Introduction: Acute paraquat (PQ) poisoning continues to be a major public health concern in many developing countries. This study was designed to evaluate the data on cases of acute PQ poisoning and compare the different variables between survivors and non-survivors.

Methods: All patients of PQ poisoning who were admitted to the poisoning emergency department during the past five years were retrospectively evaluated. The different variables that were compared between survivors and non-survivors included age and gender, the time from ingestion of PQ to hospital admission, the amount of PQ ingested, occurrence of vomiting after ingestion, the time from hospital admission to initiation of haemodialysis, the length of hospital stay and the outcomes.

Results: A total of 29 patients were evaluated. The in-hospital fatality rate was 55.2 percent. No significant differences were observed between survivors and non-survivors with regard to the patient characteristics. Most of the patients who died had ingested more than 40 mg/kg of 20 percent PQ (62.5 percent). There was a correlation between the outcome of patients and vomiting (p-value is 0.05; correlation coefficient is 0.45) and age (p-value is 0.013; correlation coefficient is 0.56).

Conclusion: A large amount of ingested PQ, vomiting and age may be important variables to consider in association with the high fatality rate of PQ poisoning.

Keywords: fatal, outcome, paraquat, poisoning

Singapore Med J 2010;51(6):496-500

INTRODUCTION

Pesticide poisoning is a major public health concern in many developing countries and accounts for up to a third of all suicides worldwide.[1,2] Paraquat (PQ) is a widely used pesticide that is applied to eliminate weeds. PQ poisoning has been observed in patients who ingest the pesticide either accidentally or intentionally as a suicide attempt.[3] PQ intoxication is more frequently fatal than poisoning caused by other pesticides. The clinical manifestation of PQ poisoning can be classified into three categories: (1) mild poisoning (less than 20 mg PQ ion per kg of body weight), in which patients often have minor gastrointestinal symptoms and usually recover fully; (2) severe poisoning (20–40 mg PQ ion per kg of body weight), in which patients develop acute renal failure, acute lung injury and progressive pulmonary fibrosis, with death occurring in 2–3 weeks as a result of respiratory failure; and (3) fulminant poisoning (more than 40 mg PQ ion per kg of body weight), in which patients develop multiple organ failure leading to death within hours to a few days after ingestion.[4,5]

The mechanisms of PQ toxicity have been evaluated by Dinis-Oliveira et al, and they have found that the lung is the main organ for the accumulation of PQ.[3] The generation of oxygen free radicals after the reduction of PQ by intracellular oxidase is responsible for pulmonary injury.[3] The management of PQ poisoning is quite difficult due to the lack of effective treatment that can be used in humans.[6] The failure of different treatments, such as treatment with absorbents, immunosuppressive therapy, radiotherapy, haemodialysis and haemoperfusion, has been reported in some studies.[5,7-10]

As acute PQ poisoning continues to be an important public health concern in many developing countries and is a common cause of mortality in presentations of poisoning at emergency departments,[11] this study was designed to evaluate the data on cases of acute PQ poisoning, and to compare the various determinants between survivors and non-survivors.

METHODS

This study was conducted at the Research Department, Isfahan University of Medical Sciences, Iran. The study protocol was reviewed and approved by the Institutional Ethics Committee. The poisoning emergency department (PED) of our university hospital is the main referral poisoning centre in the province, and is designed exclusively for the management of poisoned patients. Approximately 400 patients are admitted to the

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Table I. Frequency distribution of variables in paraquat poisoning cases (n = 29).

Variable	No. (%)
Amount of PQ ingested (mg/kg)	
< 20	5 (17.2)
20–40	2 (6.9)
> 40	17 (58.6)
Unknown	5 (17.2)
Vomiting after ingestion	
Yes	25 (86.2)
No	3 (10.3)
Unknown	1 (3.4)
Time from PQ ingestion to admission (hrs)	
< 4	21 (72.4)
4–24	4 (13.8)
> 24	4 (13.8)
Time from hospital admission to first-time HD (hrs)	
< 8	13 (44.8)
8–24	4 (13.8)
> 24	2 (6.9)
No HD	10 (34.5)
Complications (organ dysfunction)	
1 (GIT)	3 (10.3)
2 (GIT, kidney)	6 (20.7)
2 (GIT, lung)	1 (3.4)
3 (GIT, kidney, liver)	12 (41.4)
4 (GIT, kidney, liver, lung)	7 (24.1)
In-hospital outcome	
Deceased	16 (55.2)
Survived with complications	3 (10.3)
Survived without complications	0 (0.0)
Unknown (patient discharged)	10 (34.5)
Length of hospital stay (hrs)	
< 24	8 (27.6)
24–72	6 (20.7)
> 72	15 (51.7)

PQ: paraquat; HD: haemodialysis; GIT: gastrointestinal tract

department every month. We conducted a retrospective review of the medical records of 37 patients who presented at the PED with PQ poisoning between 2002 and 2006. Patients who produced a positive sodium dithionite reaction test were included in the study.

The patients were treated using gastrointestinal evacuation. It is a standard practice in our institution for PQ poisoning patients to receive gastric evacuation followed by activated charcoal (1 g/kg). Gastric evacuation was performed by inserting a small-bore nasogastric tube and suctioning the gastric contents, followed by repeated irrigation and reaspiration of 50–150 ml boluses of water until the aspirates were clear. The patients in this study also underwent haemodialysis (Fresenius 4008, Fresenius Medical Care, Homburg, Germany) and were administered with 8 mg three times a day intravenous (IV) dexamethasone (Osvah Pharmaceutical Company, Tehran, Iran), 300 mg/kg/day IV infusion acetylcysteine (Aurum Pharmaceutical Limited, Romford Essex, England), 150 mg/hr IV infusion vitamin C (Daroupakhsh Pharmaceutical Company, Tehran, Iran), and 100 U/ml twice a day intramuscular vitamin E (Osvah Pharmaceutical Company, Tehran, Iran).

The data was manually collected from the patients' records. The information recorded included age, gender, time from the ingestion of PQ by the patient to hospital admission, the amount of PQ ingested, occurrence of vomiting after ingestion, the time from hospital admission to the initiation of haemodialysis for the first time, the length of hospital stay and the outcomes (died, survived with complications, survived without complications). The variables were compared between survivors and non-survivors.

The results were presented as mean ± standard error and percentage, where appropriate. The differences between survivors and non-survivors were tested using the *t*-test for continuous variables. The relationships between the outcomes and the variables were evaluated using the Spearman's correlation test. The data was analysed using the Statistical Package for the Social Sciences version 13.0 (SPSS Inc, Chicago, IL, USA) and MedCalc (MedCale Software Inc, Mariakerke, Belgium) statistical software. A p-value < 0.05 was considered to be statistically significant.

RESULTS

A total of 37 patients presented with PQ poisoning at the PED during the five years of study. The records of eight patients were excluded, as these patients had a negative dithionate test on admission and during their stay in the hospital. All cases were the result of the intentional ingestion of PQ commercial products. There were more male (n = 21) than female (n = 8) patients. Most patients were 18–40 years of age (51.7%). 27.6% of the patients were < 18 years of age, and 20.7% were > 40 years of age. The mean age was 27.58 ± 2.39 years, with a minimum and maximum age of 12 and 66 years, respectively.

The results for the amount of PQ ingested, occurrence of vomiting after ingestion, time from ingestion of PQ to hospital admission, time from presentation to the initiation of haemodialysis for the first time, complications, in-hospital outcomes and the length of hospital stay are presented in Table I. Patients with unknown outcomes (n = 10) who made their own decision to be discharged from the hospital, and whose mean length of hospital stay was 107.2 ± 18.02 hours, were excluded from further analysis. Among the remaining cases (n = 19), 16 poisoning-related fatalities were reported, and these were predominantly

Table II. Comparison of the variables between survivors and non-survivors in paraquat poisoning (n = 19).

Variable	(Mean ± SE)		p-value
	Survivors	Non-survivors	
Age (yrs)	15.66 ± 0.88 (n = 3)	27.62 ± 2.99 (n = 16)	0.11
Paraquat amounts (ml)	10 ± 0.00 (n = 2)	300 ± 147.25 (n = 14)	0.48
Time from ingestion to admission (hrs)	1.83 ± 0.16 (n = 3)	15.65 ± 6.34 (n = 16)	0.37
Time from hospital admission to first-time HD (hrs)	3.83 ± 1.01 (n = 3)	8.15 ± 2.14 (n = 10)	0.31

SE: standard error; HD: haemodialysis

Table III. Frequency distribution of the variables between survivors and non-survivors in paraquat poisoning (n = 19).

Variable	No. (%)	
	Survivors	Non-survivors
Amount of paraquat ingested (mg/kg)		
< 20	0 (0)	4 (25)
20–40	2 (66.7)	0 (0)
> 40	0 (0)	10 (62.5)
Unknown	1 (33.3)	2 (12.5)
Vomiting after ingestion		
Yes	2 (66.7)	15 (93.8)
No	1 (33.3)	0 (0)
Unknown	0 (0)	1 (6.2)
Time from ingestion to admission (hrs)		
< 4	3 (100)	11 (68.7)
4–24	0 (0)	2 (12.5)
> 24	0 (0)	3 (18.8)
Time from hospital admission to first-time HD (hrs)		
< 8	3 (100)	8 (50)
8–24	0 (0)	1 (6.2)
> 24	0 (0)	1 (6.2)
Did not undergo HD	0 (0)	6 (37.6)
Complications (organ dysfunction)		
1 (GIT)	1 (33.3)	0 (0)
2 (GIT, kidney)	0 (0)	2 (12.5)
2 (GIT, lung)	0 (0)	1 (6.2)
3 (GIT, kidney, liver)	2 (66.7)	7 (43.8)
4 (GIT, kidney, liver, lung)	0 (0)	6 (37.5)
Length of hospital stay (hrs)		
< 24	0 (0)	7 (43.8)
24–72	0 (0)	3 (18.7)
> 72	3 (100)	6 (37.5)

HD: haemodialysis; GIT: gastrointestinal tract

male patients (66.7%). Most of the patients who did not survive had ingested more than 40 mg/kg of 20% PQ (62.5%). The comparison between survivors and non-survivors with respect to the different variables is outlined in Tables II and III. The correlations between the variables and outcomes were evaluated. Among the factors studied, vomiting ($p = 0.05$, correlation coefficient = 0.45) and age ($p = 0.013$, correlation coefficient = 0.56) were found to be associated with the outcome of poisoned patients. Discrimination was tested using the area under the receiver operating characteristic (ROC) curves.[12] The area under the curve, between 0.7 and 0.8, was classified as "acceptable" and between 0.8 and 0.9 as "excellent" discrimination.[13] The area under the ROC curve and the sensitivity and specificity for age to predict fatality was calculated. For the prediction of fatality, the best cut-off point for age was 17 years (area under curve 0.937 ± 0.059, 95% confidence interval [CI], 0.73–0.99; $p < 0.0001$), sensitivity 93.75 (95% CI, 69.7–99) and specificity 100 (95% CI, 30.5–100).

DISCUSSION

Our results show that the mortality rate was high in PQ poisoning cases, which may be attributed to the large quantity (> 40 ml/kg) of 20% PQ that was ingested by our patients. The amount of the toxin, the PQ formulation and the circumstances in which the poisoning occurred are important factors in predicting mortality, as suggested by Pronczuk de Garbino.[14] The fatality toxicity index (death/exposure) due to PQ self-poisoning has been reported to be higher than that due to other common pesticides in a study that was related to product toxicity and the severity of the poisoning.[11] Higher patient fatality ratios due to PQ ingestion have also been shown in other studies.[15,16]

Although the mechanisms of PQ toxicity have been evaluated,[3] no specific therapy has been shown to reduce mortality.[17] The efficacy of gut lavage, activated charcoal, haemodialysis and haemoperfusion as treatments for PQ poisoning has been questioned in the studies of Okonek et al[18] and Gaudreault et al.[19] Previous studies have also shown that treatment with cyclophosphamide and methylprednisolone could reduce the mortality rate in PQ patients; however, some studies have disagreed with these results.[5,20-26]

There was a significant but weak relationship between the patient's outcome and vomiting in our study. Some studies have evaluated the role of the prevention of PQ absorption by using a potent emetic in PQ formulations; however, the efficacy of these measures on PQ fatality has not been definitively demonstrated, which may be due to the large amount of PQ ingested.[27-32] Recently, a study by Wilks et al reported an improvement in the survival rate

after PQ ingestion following the introduction of a new formulation that potentially slows the absorption of PQ and provides more time for the emetic to be effective.[2] Our results also showed that there was a relationship between patient outcome and age. However, the relationship was weak, and this can be attributed to our small sample size.

In conclusion, PQ poisoning remains a problem mainly among the young, with a gender ratio that is skewed toward males. A large amount of ingested PQ, vomiting and age may be considered important variables in the high fatality rate of PQ poisoning. Our findings may not be significantly different from what is already known. However, this study shows that PQ poisoning is still a concern in developing countries. It may be useful to educate public health professionals and the general public about the serious consequences of exposure to this agent, the prevention of pesticide misuse and hence, the prevention of acute severe pesticide poisoning (e.g. by reducing the notoriety of tools for suicide, ensuring secure access for all pesticides/chemicals).

One limitation of our retrospective study is that the number of patients was too small to define and compare the role played by the different prognostic variables between survivors and non-survivors. Therefore, further prospective studies over a longer period of time are required in order to describe the relative importance of determinants among survivors and non-survivors in PQ poisoning. Our current treatment was also unable to reduce fatality in PQ poisoning cases. Since PQ poisoning is commonly reported in our department, there is an urgent need for the development of preventive approaches and large prospective clinical trials on the effects of different combinations of treatment.

ACKNOWLEDGEMENTS

The authors would like to thank the members of the Anaesthesiology Department, Isfahan University of Medical Sciences and all the staff of the Poisoning Emergency Department for their invaluable support.

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