ORIGINAL ARTICLE

Medical Management and Outcome of Paraquat Poisoning in Ahvaz, Iran: A Hospital-Based Study

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Abstract

Background: Paraquat (PQ) poisoning is highly fatal; and therefore, clinicians should be familiar with prompt approach to and poor prognostic features of this type of poisoning. Hence, in this study, clinical profile, management and outcome of a series of patients with PQ poisoning are presented.
Methods: A retrospective review of medical records of patients poisoned with PQ who were treated at Clinical Toxicology Department of Razi Hospital in Ahwaz, Iran during 2005 to 2008 was performed.
Results: Forty-two patients (66.7% men) were studied. Majority of them (83.3%) were between 15-29 years of age. Most of PQ poisonings occurred following suicidal ideation (39 patients; 92.9%). The most common on-admission clinical findings of the patients were vomiting (69%) and respiratory distress (47.6%). Activated charcoal was given to 35 patients (83.3%). N-acetyl cysteine (100 mg/kg IV stat), vitamin E (100 IU daily IV) and vitamin C (500 mg daily IV) were given to all patients. Exploratory endoscopy for plausible mucosal ulcers was carried out for 23 patients (54.8%). Pantoprazole (40 mg twice daily) was given to all patients and for 7 patients with upper gastrointestinal (GI) irritation and GI bleeding, higher doses of pantoprazole (8 mg/hour) was administered. All patients received pulse therapy with methyl prednisolone (1g daily for three days) and cyclophosphamide (15 mg/kg daily for two days). Twenty patients died. Comparing death and survival, death was significantly higher in patients with respiratory distress (100 vs. 0.0 %, $P < 0.001$), renal dysfunction (85.0 vs. 9.1 %, $P < 0.001$) and hepatic dysfunction (75.0 vs. 4.5 %, $P < 0.001$).
Conclusion: PQ poisoning creates a life-threatening clinical situation, which requires quick and proper treatment. Based on this research, mortality rate is greater in the presence of renal, hepatic and respiratory dysfunction.

Keywords: Disease Management; Herbicides; Mortality; Paraquat; Poisoning

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INTRODUCTION

Poisoning with pesticide agents is a major public health concern in many developing countries which accounts for up to one-thirds of all suicides throughout the world (1,2). Paraquat (PQ), a widely used herbicide, is a dipyridylium quaternary ammonium salt. It is commercially available in 20% concentrate, 2.5% granules, and 0.2% aerosol formats. PQ can be rapidly absorbed through oral or inhalational exposure, while absorption through the intact skin is generally very limited. The exact mechanism of PQ toxicity is not completely known; however, clinical features are mainly due to intracellular toxic effects (3-5). Several studies have suggested that PQ undergoes redox-cycling and subsequently generates superoxide anion, singlet oxygen and other free radicals, leading to cellular NADPH depletion and lipid peroxidation of cell membranes (6,7). Generation of highly reactive oxygen and nitrite species results in toxicity in most organs, but the toxicity is particularly severe in the lungs as PQ is taken up against a concentration gradient into the lung tissue and predominantly by the type II pneumocytes (8,9).

Clinical manifestations of PQ poisoning are categorized into mild, moderate, and severe stages based on the exposure dose. Mild poisoning (less than 20 mg PQ ion/ kg) is often associated with minor gastrointestinal symptoms and recovery is usually complete. In severe poisoning (20–40 mg PQ ion /kg), patients develop acute renal failure, acute lung injury and progressive pulmonary fibrosis, with death occurring within 2-3 weeks because of respiratory failure. Fulminant poisoning (> 40 mg PQ ion/ kg), causes multiple organ failure leading to death within several hours to few days after ingestion (10-13).

Pesticide poisoning comprises 2-3% of reported poisoning cases to Iranian Drug and Poison Information Centers (14); however, only a limited number of them are due to PQ

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ingestion (15). Nonetheless, PQ poisoning, either intentional or accidental, is highly fatal; and therefore, clinicians should be familiar with prompt approach to and poor prognostic features of this type of poisoning (10,15,16). Hence, in this study, clinical profile, management and outcome of a series of patients with PQ poisoning treated at Razi Hospital in Ahwaz, Iran, during 2005 to 2008 are presented.

METHODS

Study design and subjects

In this study, a retrospective review of medical records of patients poisoned with PQ who were treated at Clinical Toxicology Department of Razi Hospital (a referral medical setting for poisoning treatment in southwest Iran) during 2005 to 2008 was performed. Diagnosis of PQ poisoning was confirmed based on patients' history, clinical manifestations and laboratory analysis. Data collected for this study included age, gender, marital status, place of residence (urban or rural), elapsed time from PQ ingestion to hospital admission, clinical manifestations of the patients, treatments delivered to the patients and the outcome of patients. The study protocol was reviewed and approved by the institutional ethics committee.

Statistical analysis

Data were analyzed using the Statistical Package for the Social Sciences (SPSS) version 18.0 (SPSS Inc., Chicago, IL, USA). For outcome analysis, Fisher's exact test was applied with the level of significance set at $P < 0.05$.

RESULTS

Sociodemographic profile and circumstances of poisoning

During the study period, 42 patients (66.7% men) with PQ poisoning were treated at Razi Hospital. Majority of the patients (83.3%) were between 15-29 years of age (Table 1). Thirty patients (71.4%) were unmarried. Most of PQ poisonings occurred following suicidal ideation (39 patients; 92.9%). According to place of residence, 22 victims (52.4%) lived in rural areas, all of whom were farmers. The majority of patients (66.7%) arrived in the hospital within less than 6 hours of poison ingestion.

Clinical findings and treatments

The most common on-admission clinical findings of the patients were vomiting (69%), respiratory distress (47.6%), renal dysfunction (45.2%) and liver dysfunction (38.1%) (Figure 1).

Management of paraquat poisoning has remained mainly supportive. Activated charcoal was given to 35 patients (83.3%). Forced gastric lavage was not performed for the patients due to the risk for perforation in the presence of corrosive mucosal damage. Fluid and electrolyte therapy to replace gastrointestinal (GI) losses was administered to all patients. For ameliorating the toxic effects produced by paraquat, antioxidants including N- acetyl cysteine (100 mg/kg IV stat), vitamin E (100 IU daily IV) and vitamin C (500 mg daily IV) were given to all patients. To investigate plausible severe GI mucosal injuries which are candidate for preventive surgical treatment, endoscopy was carried out for 23 patients (54.8%). Chlorhexidine mouthwash was given to 7 patients (16.7%) with oral and pharyngeal mucosal ulcers.

Table 1. Socio-demographic features and circumstances of poisoning in patients with paraquat poisoning treated at Razi Hospital during 2005 to 2008 (n = 42)

Variable	N (%)
Gender	
Female	14 (33.3)
Male	28 (66.7)
Age group (year)	
15-29	35 (83.3)
30-45	6 (14.3)
> 45	1 (2.4)
Marital status	
Single	30 (71.4)
Married	12 (28.6)
Intention of poisoning	
Suicidal	39 (92.2)
Accidental	3 (7.1)
Place of residence	
Rural	22 (52.4)
Urban	20 (47.6)
Time elapsed from ingestion to hospital admission	
< 6 hours	28 (66.7)
6-24 hours	8 (19.0)
> 24hours	6 (14.3)

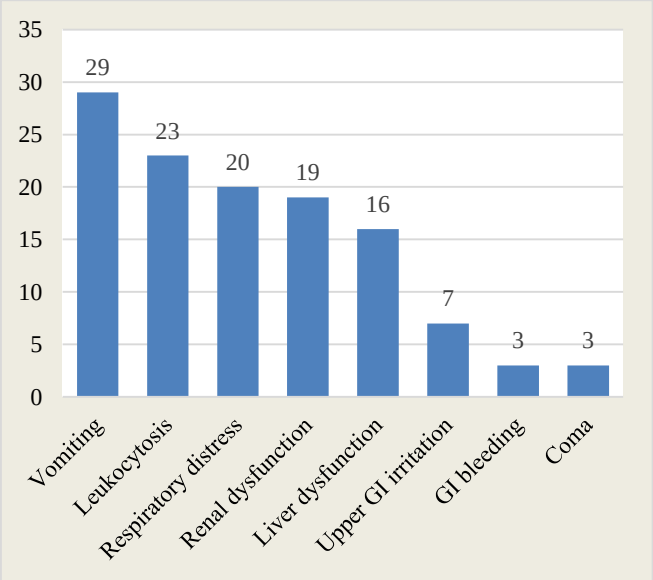

Figure 1. On-admission clinical findings of the patients (n = 42)

For reducing the complications of caustic GI mucosal injuries, pantoprazole (40 mg twice daily) was given to all patients and for 7 patients with upper GI irritation and GI bleeding, higher doses of pantoprazole (8 mg/hour) was administered.

For reducing the PQ-induced progressive systemic damages, all patients received pulse therapy with methyl prednisolone (1g daily for three days) and cyclophosphamide (15 mg/kg daily for two days). For removal of the poison from the blood circulation, twenty-four patients (57.1%) including twenty who later died underwent hemodialysis. The majority of patients (34 patients, 80.9 %) required ICU admission.

Outcomes and prognosis analysis

Because of complications, 20 patients died. To evaluate the impact of clinical findings and circumstances of poisoning on PQ poisoned patients' outcomes, only variables with adequate frequency (n > 10) for statistical analysis were compared between death and survival outcomes (Table 2). Comparing deceased and survived cases, death was significantly higher in patients with respiratory distress (100 vs. 0.0 %, P < 0.001), renal dysfunction (85.0 vs. 9.1 %, P < 0.001) and hepatic dysfunction (75.0 vs. 4.5 %, P < 0.001). Although, leukocytosis and vomiting were higher among deceased cases, they had no significant impact on patients' survival. Moreover, ICU admission requirement was a poor prognostic factor as it was higher in deceased cases compared with survived ones (100 vs. 63.6%, P = 0.004). In addition, comparing death and survival, the frequency of patients who were admitted to the hospital after 24 hours of PQ ingestion was higher in death outcome, though the difference was only close the level of significance (25.0 vs. 4.5 %, P = 0.087)

DISCUSSION

PQ poisoning is an extremely frustrating condition to be managed clinically due to high rate of associated morbidities and no available antidote (17-20). In the present study, most of the victims were young farmers. This can be due to the easy availability of pesticides for this working class (21). The most common clinical findings seen in our patients were vomiting, respiratory dysfunction, renal dysfunction and liver dysfunction. Goudarzi et al similarly reported vomiting, epigastric pain, increased creatinine and increased liver enzymes as the most common clinical manifestations in a series of PQ poisoned patients in Shiraz (15).

According to our results, nearly half of the PQ ingestions (47.6%) resulted in death. This figure is comparable to the death rates reported in other studies carried out by Goudarzi et al in Shiraz, Iran (51.9%), Sabzghabaee et al in Isfahan, Iran (55.2%), and Hwang et al in Choongnam, South Korea (43.8%) (10,15,22). However, the death rates in the studies by Nagami et al in Japan (79.2%) and Gil et al in Cheonan, South Korea (70.7%) were much higher (23,24). This may be attributed to the fact that the patients included in the Nagami et al and Gil et al's study were somehow older compared with the present and the above-mentioned studies (10,15,22-24). In general, as can be seen, PQ poisoning is associated with high mortality. This is mainly due to the fact that there is no specific antidote for PQ. Moreover, extracorporal facilities (hemoperfusion) are not available in all medical settings especially in developing countries (25,26).

A large number of methods intended to eliminate PQ toxicity have been investigated (8,27). Nonetheless, there is no convincing controlled evidence that any of them are unequivocally useful. The most important determinant of survival after ingestion is early treatment. The initial

Table 2. Outcome analysis of the PQ poisoned patients treated at Razi Hospital, Ahvaz

Variables	Outcome		P value[4]
	Death (n = 20)	Survival (n = 22)	
Vomiting; n (%)	15 (75.0)	14 (63.6)	0.514
Leukocytosis[1]; n (%)	13 (65.0)	10 (45.5)	0.232
Respiratory distress; n (%)	20 (100)	0 (0.0)	< 0.001
Renal dysfunction[2]; n (%)	17 (85.0)	2 (9.1)	< 0.001
Liver dysfunction[3]; n (%)	15 (75.0)	1 (4.5)	< 0.001
Time elapsed from ingestion to hospital admission; n (%)			
< 24 hours	15 (75.0)	21 (95.5)	0.087
≥ 24 hours	5 (25.0)	1 (4.5)	
Intention of poisoning; n (%)			
Suicide	18 (90.0)	21 (95.5)	0.598
Accidental	2 (10.0)	1 (4.5)	
ICU admission requirement; n (%)			
Yes	20 (100)	14 (63.6)	0.004
No	0	8 (36.4)	

[1] White blood cell count > 11,000 cells/mm^3
[2] Increased creatinine
[3] Increased liver enzymes
[4] Analyzed with Fisher's exact test

treatment priorities for PQ poisoning are administration of an adsorbent (such as activated charcoal) to neutralize the ingested PQ (25-27). Secondly, because paraquat is a caustic agent and so there is a risk for perforation in the presence of corrosive mucosal damage (28), early gastric lavage might be helpful but emesis is not indicated (25-27). Moreover, for determining the patients with severe mucosal ulcers who are candidate for preventive surgical treatment, endoscopy is better to be taken into account (29). Third, intermittent hemoperfusion and hemofiltration should be considered (25-27); and in the absence of them, hemodialysis is an alternative but its efficacy is limited (27). For prevention of PQ-induced underlying oxidative damages, treatment with antioxidants might be effective, but its efficacy has not been proven (25,26,30). Finally, immunosuppressive therapy with methyl prednisolone and cyclophosphamide which can arrest oxidative damages has been shown to significantly reduce the mortality (27,31).

In the present study, we analyzed the prognostic ability of some clinical and poisoning-related variables. Renal dysfunction, hepatic insufficiency, respiratory distress and ICU admission requirement were shown to be the strongest risk factors for poor prognosis in PQ poisoning. Goudarzi et al similarly ascertained respiratory distress, increased creatinine and increased liver enzymes as predictive factors for death (15). Lee et al, likewise, demonstrated that patients with renal or hepatic dysfunction have significant risks for fatality (32). Similar to these findings Sabzghabaee et al found that kidney, lung and/or liver involvements following PQ ingestion are higher among non-survived cases (10). Although Goudarzi et al showed that suicidal intent is associated with higher mortality (15), we could not establish such relationship in this study.

LIMITATIONS

The diagnosis in the present study was mostly based on patients' history and clinical examination. Serum levels of PQ was not measured in the majority of patients.

CONCLUSION

PQ poisoning creates a life-threatening clinical situation, which requires quick and proper treatment. Based on this research, mortality rate is greater in the presence of renal, hepatic and respiratory dysfunction. Clinicians should consider these manifestations as the indicators for administration of more vigilant observation and more aggressive care.

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Conflict of interest: None to be declared.

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