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A study on Clinical features and management of Paraquat poisoning

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Abstract

Introduction: Paraquat is a widely used herbicide and a potent toxin. Ingestion, rather than inhalation, is the typical route of exposure associated with human toxicity. There have been systemic reactions following skin exposure after direct exposure to the skin (soaking of the skin with paraquat) or when the skin integrity has been breached (preexisting skin lesions or burn). Most paraquat deaths result from suicidal intent. Although paraquat ingestion leads to acute gastrointestinal tract necrosis and multiorgan failure, the lung is the target organ for toxicity among those surviving the immediate postingestion period.

Material and Methods: This is a retrospective study conducted in the Department of Critical Care at NRI Medical College & General Hospital, Guntur. The study included patients with the ages above 14 years old who were presented to the Emergency Department with paraquat poisoning. This includes patients who were self-admitted or with witness account of paraquat exposure (ingestion, inhalational, mucosal or skin contact).

Results: In our study, most of the patients were belongs to 26-35 years 17(48.5) followed by 18-25 years 9 (25.7), 36-45 years 6 (17.1), 46-55 years and more than 56 years were 5.7% and 2.8% respectively. The majority were male (n=29, 82.8%) and female (n=6, 17.1%) were least. The main symptoms and signs of studied patients include nausea (94.2%); vomiting (88.5%); Abdominal pain (91.4%); Paraquat tongue (88.5%), Oliguria (45.7%); Jaundice (37.1%), Respiratory distress (2.8%). For survived and non-survived patients, the Amount of ingested paraquat (mL) the mean ± SD was 25.6±5.6 ml and 295±28 ml respectively. The difference was statistically significant (P=0.001).

Conclusion: It is important to establish the diagnosis early and to pursue aggressive decontamination and prevention of further absorption. Increased awareness of the clinician and availability of the laboratory diagnostic methods will definitely help in successful

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management of paraquat poisoning. Paraquat poisoning is still a concern in developing countries. It may be useful to educate public health professionals and the general population about the serious consequences of exposure to this toxic agent. Paraquat poisoning is still no cure.

Keywords: Paraquat poisoning, Clinical features, Management

Introduction

Paraquat is a widely used herbicide and a potent toxin. Ingestion, rather than inhalation, is the typical route of exposure associated with human toxicity. [1] There have been systemic reactions following skin exposure after direct exposure to the skin (soaking of the skin with paraquat) or when the skin integrity has been breached (preexisting skin lesions or burn). [2]

Most paraquat deaths result from suicidal intent. Although paraquat ingestion leads to acute gastrointestinal tract necrosis and multiorgan failure, the lung is the target organ for toxicity among those surviving the immediate postingestion period. Diquat, a related dipyridyl herbicide, does not cause the lung injury associated with paraquat, although poisoning can lead to renal failure and cerebral hemorrhage. [3]

The pulmonary toxicity of paraquat, in contrast to its gastrointestinal effects, does not reflect caustic irritant injury. The major lung effect of paraquat toxicity is the development of pulmonary edema, usually observed 24 to 48 hours after ingestion. [4] The pulmonary edema may evolve to a condition resembling ARDS, associated with histopathologic findings similar to those of DAD, which may progress to an accelerated, chemically induced pulmonary fibrosis. [5]

After stabilization following acute multiorgan toxic effects, disease progression is marked by rapidly worsening respiratory distress, hypoxemia, and a restrictive ventilatory defect, with decreased lung compliance and diffusing capacity, ending in death from ventilatory failure within days to weeks. Survivors may demonstrate modest and slow improvement in lung function. [6]

The mechanism of paraquat toxicity is attributed to the generation of superoxide radicals that may be partly iron dependent. Consistent with an oxidant mechanism, supplemental oxygen and radiation therapy may worsen the outcome; there are no known antidotes for paraquat poisoning, and enhanced elimination such as by hemoperfusion has not demonstrated a clear benefit. [7] Plasma paraquat levels can be determined and may have a use in predicting outcome. [8] Death results from multiorgan failure, which usually happens within 1 to 2 weeks but may be observed up to 6 weeks after ingestion. [9]

Aim: Paraquat is a contact herbicide which is highly toxic to human. Deliberate self-poisoning with paraquat continues to be a major public health concern in many developing countries. This study aimed to evaluate the data on cases of acute paraquat poisoning and to compare different variables between survivors and non-survivors.

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Material and Methods

This is a retrospective study conducted in the Department of Critical Care at NRI Medical College & General Hospital, Guntur.

Inclusion criteria

The study included patients with the ages above 14 years old who were presented to the Emergency Department with paraquat poisoningdu. This includes patients who were self-admitted or with witness account of paraquat exposure (ingestion, inhalational, mucosal or skin contact).

Data were obtained manually from the patient's medical records. The information recorded includes age, gender, marital status, living place, the route of intoxication, amount ingested, admission date and place, the length of hospital stay, symptoms and signs, laboratory findings, treatment received and outcomes.

Table 1. Symptoms and signs of acute Paraquat intoxication, according to the severity of intoxication

Severity of intoxication	Ingested amount (mL)	Symptoms	Signs
Mild	< 10	No specific symptom	No specific sign
Moderate	10-40	Sore tongue Shortness of breath Agitation Abdominal discomfort Head lightness	Tachypnoea Tachycardia Increased serum creatinine Oral mucosa necrosis
Severe	> 40	Sore tongue Shortness of breath Hiccup* Agitation Confusion†	Tachypnea Tachycardia Increased serum creatinine Oral mucosa necrosis Jaundice

*Hiccups generally occur when the ingestion amount is > 100 mL and far ominous symptoms; †Confusion is usually accompanied by death within a few days.

Statistical analysis

The data was analyzed using SPSS version 20. Descriptive statistics were presented as mean ± standard deviation (SD) and percentage, where appropriate, to summarize the demographic characteristics, clinical features and outcomes of the cases. The variables were also compared between survivors and non-survivors. The t test was used to investigate the differences of quantitative variables. The relationships between categorical variables and the outcomes were evaluated using Chi square test where appropriate. In all cases, a confidence interval of 95% and a significance level of 5% ($P<0.05$) was considered.

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Results

In table 1, most of the patients were belongs to 26-35 years 17(48.5) followed by 18-25 years 9 (25.7), 36-45 years 6 (17.1), 46-55 years and more than 56 years were 5.7% and 2.8% respectively.

Table 1. Distribution of age of the patients with paraquat poisoning (n=35)

Age Group in years	Frequency	Percentage
18-25	9	25.7
26-35	17	48.5
36-45	6	17.1
46-55	2	5.7
>56	1	2.8
Total	35	100

Table 2: Distribution of Gender

Gender	Frequency	Percentage
Males	29	82.8
Female	6	17.1
Total	35	100

In table 2, the majority were male (n=29, 82.8%) and female (n=6, 17.1%) were least.

Table 3. Baseline characteristics of patients with paraquat poisoning (n=35)

Reasons for self-harm	Frequency	Percentage
Alcohol abuse	23	65.7
Disease	4	11.4
Economic crises or occupation-related insecurity	5	14.2
Marital conflict	3	8.5
Total	35	100

Table 4. Clinical features of the patients (n=35) noted at the medical college hospital

Clinical feature	Frequency	Percentage
Vomiting	31	88.5
Nausea	33	94.2
Abdominal pain	32	91.4
Shock	19	54.2
Paraquat tongue	31	88.5
Odynophagia	01	2.8
Oliguria	16	45.7
Jaundice	13	37.1
Respiratory distress	01	2.8

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In table 4, the main symptoms and signs of studied patients include nausea (94.2%); vomiting (88.5%); Abdominal pain (91.4%); Paraquat tongue (88.5%), Oliguria (45.7%); Jaundice (37.1%), Respiratory distress (2.8%).

Table 5. Amount of ingested paraquat (mL) and Duration of hospital stay (days) (N=35)

Characteristics	Number (%) of patients		
	Survivor	Non-survivor	P value
Amount of ingested paraquat (mL)	25.6±5.6	295±28	0.001
Duration of hospital stay (days)	6.65±1.25	3.92±0.94	0.025

In table 5, For survived and non-survived patients, the **Amount of ingested paraquat (mL)** the mean ± SD was 25.6±5.6 ml and 295±28 ml respectively. The difference was statistically significant (P=0.001).

Table 6. Clinical characteristics and outcome of paraquat intoxicated patients (N=35)

Characteristics	Number (%) of patients		
	Survivor	Non-survivor	P value
Admission service			
Ward	18 (72)	7 (28)	0.008
ICU	1 (16.7)	5 (83.3)	
First ward then ICU	1 (25)	3 (75)	
Leukocytosis			<0.001
Yes	1 (7.7)	12 (92.3)	
No	18 (81.8)	4 (18.2)	
Increased serum creatinine			0.001
Yes	6 (28.6)	15 (71.4)	
No	13 (92.9)	1 (7.1)	
Acute hepatitis			<0.001
Yes	0 (0)	10 (100)	
No	20 (80)	5 (20)	

Discussion

Paraquat is a nonselective contact herbicide of great toxicological importance. The in-hospital fatality rate of Paraquat poisoning is approximately 55%, with no significant differences between survivors and non-survivors with respect to the patient characteristics. [10] As Vale et al. [11] reported, three degrees of Paraquat intoxication have been differentiated: (1) mild poisoning (occurs after ingesting <20 mg of Paraquat ion per kg body weight), which usually results in full recovery; (2) moderate-to-severe poisoning (20–40 mg of Paraquat ion per kg body weight), which is fatal in the majority of cases 2–3 weeks after ingestion; and (3) acute fulminant poisoning (>40 mg of Paraquat ion per kg body weight),

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which is fatal in the majority of cases within hours to days of ingestion. However, despite serious complications, including acute renal failure, infection, pulmonary infiltration, and pleural effusion, they all survived.

After being ingested, Paraquat is rapidly distributed to organs and tissues, particularly the lungs. The lung Paraquat concentration is more than 10 times higher than that in the plasma. It has been suggested that the mechanism is primarily related to oxidative damage, reactive oxygen species, immune activation, inflammatory mediators. [12] At present, oxygen is not a part of treatment, because too much oxygen can rapidly promote pulmonary changes through oxidation.

Paraquat is excreted primarily by kidneys, and therefore, hemoperfusion has often been indicated as an appropriate step for treatment and is considered 4–6 times more effective than hemodialysis. [13] Additionally, it is believed that hemoperfusion should be started as early as possible after Paraquat poisoning, and should be continued for >10 h. [14] It is difficult, however, to completely remove Paraquat through hemoperfusion, since patients often swallow several times the lethal dose, and by the time hemoperfusion is administered the Paraquat has already spread to lung tissue and other vital organs, and only a small amount of Paraquat is remained in the blood circulation. Blood purification can significantly decrease the levels of inflammatory cytokines and oxygen free radicals, and improve the physiological environment. Every time, hemoperfusion is continued about 4 h until the result of urine Paraquat detection is negative.

Currently, many experts point out that therapy combining glucocorticoid and cyclophosphamide should be effective to treat poisoning. [15] Activation of mononuclear macrophages and granular leukocytes causes acute lung injury and pulmonary fibrosis. [16] By stabilizing cell membranes and fighting against lipid peroxidation and non-specific immune suppression, glucocorticoid reduces leukocytes gathering in the damaged area, decreases collagen activity and improves respiratory function. [17] Cyclophosphamide also plays an important role in the cellular and humoral immune response, and reduces the severity of inflammation. [18] In a word, therapy combining glucocorticoid and cyclophosphamide for Paraquat poisoning can reduce the severity of inflammation, decrease the number of leukocytes to slow the process of pulmonary fibrosis, and reduce mortality in patients with moderate-to-severe Paraquat poisoning. [19] However, limited evidence exists regarding the appropriate therapeutic dose and duration of treatment. We believe that early large-dose glucocorticoid therapy can produce its best effect, and a combination with a total dose of 4 g cyclophosphamide may be more effective in treating patients with severe Paraquat poisoning. Additionally, in order to ensure the immunosuppressive effect, we suggest increasing the dose and administering these drugs after hemoperfusion.

In most cases, since patients were sent to our hospital over 6 h after Paraquat ingestion, the Paraquat had already spread to various tissues and organs, resulting in a very low concentration of Paraquat in the blood. In these cases, the degree of Paraquat poisoning is

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identified via the assessment of dosage ingested and clinical features presented. In our study, all three cases developed acute renal failure within a few days, and their chest CTs showed similar changes (pulmonary infiltration, pleural effusion, and pulmonary fibrosis). They were all treated by similar compound methods and survived. Our treatment strategies included performing hemoperfusion six times, together with hemodialysis to cure acute renal failure; early large-dose glucocorticoid therapy, combining with an adequate dose of cyclophosphamide (about 4 g of total dose); giving several kinds of antioxidants and symptomatic treatments.

Conclusion

There is no specific antidote available for paraquat poisoning. It is important to establish the diagnosis early and to pursue aggressive decontamination and prevention of further absorption. Increased awareness of the clinician and availability of the laboratory diagnostic methods will definitely help in successful management of paraquat poisoning. Paraquat poisoning is still a concern in developing countries. It may be useful to educate public health professionals and the general population about the serious consequences of exposure to this toxic agent. Paraquat poisoning is still no cure.

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