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Original Research

Manifestation, complications and clinical outcome in paraquat poison? A hospital based study in a rural area of Karnataka

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Summary

Background: Paraquat is a broad spectrum liquid herbicide, leading to severe and often fatal toxicity. Most cases of intoxication, especially in third-world countries are due to suicidal attempts rather than homicidal or accidental exposure, because of its widespread availability and relative low cost. Diagnosis is often difficult in the absence of proper history, nonspecific clinical features, and lack of diagnostic tests.

Aim: To describe the variability in presentation, primary outcome from intentional poisoning and to review its impact on morbidity and mortality of poisoning.

Method: We report a case series of eight patients with paraquat poisoning who presented predominantly with pain in throat and vomiting.

Results: Out of eight cases six patients died despite intensive treatment. Most deaths occurred within in two weeks.

Conclusion: Paraquat poison is highly lethal or deadly poison with very high mortality rate of around 70 to 80%. Also presentation may be variable and sometimes patient may present with mild symptoms with normal vitals or may remain asymptomatic for first few days. Although even in such cases morbidity and mortality of poison may be very high.

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INTRODUCTION

Paraquat (1,1'-dimethyl-4,4'-bipyridylium dichloride) is widely used herbicide. Globally it is the second highest-selling weedicide. It is usually marketed either as a 20% solution or in a granular form. Its herbicidal properties were discovered in 1950s and first marketed in 1962. [1] The rate of increase in pesticide and herbicide use is relatively high in India. It is available in both solid and liquid forms. [2]. Toxicity is usually seen following ingestion, and may range from mild ingestion of < 20 mg paraquat ion/kg body weight=10ml of 20% concentrate to fulminant >40 mg paraquat ion/kg body weight ≥20ml, with the latter commonly proving fatal. Ingestion of paraquat poison in larger doses causes rapid death, but even smaller doses can result in lung fibrosis and can be fatal [3]. Paraquat is stored and only slowly released from different tissues. The poison accumulates slowly in lung via energy dependent

process. Generation of reactive oxygen species and subsequent lipid peroxidation is responsible for lung injuries like pulmonary edema, interstitial pneumonia and lung fibrosis in paraquat poisoning [4]. Much remains to be learned about role of intra cellular and extracellular anti oxidants in paraquat poisoning [2]. In addition to intense local irritation of the mouth, oropharynx and oesophagus, multiple organ (cardiac, respiratory, hepatic and renal) failure may occur. Pulmonary features predominate and are the usual cause of death [5]. The present study was conducted to find morbidity, mortality and describe variability in presentation. Death may occur up to 30 days after ingestion, so patients should be kept under observation even if they are asymptomatic or with minimal symptom and aggressive treatment should be used as mortality is very high.

MATERIAL AND METHODS

This prospective study was done in Adichunchangiri institute of medical science and Hospital, from June 2012 to November 2013 after obtaining clearance from the Institutional Ethical committee. All the patients with alleged history of consumption of paraquat were included in this study. Patients who consumed paraquat presented to Emergency Room [ER] were managed according to the protocol. The length of hospital stay ranged from 1 to 30 days and six out of eight patients died during hospitalisation. The diagnosis was based on the history, verification of the ingested herbicide, serum and urine examination for the presence of paraquat. Samples were stored at -20°C until analysis and method for analysis was Enzyme-Linked Immunosorbent Assay.

RESULTS

Out of Eight patients who had exposure to paraquat were included in this study. Six patients were females between 20 to 40 years of age. All of the eight patients had paraquat solution ingested for suicidal attempt. The degree of poisoning was assessed by the quantity of paraquat concentrate ingested. Four patients had severe intoxication to paraquat, one case has moderate intoxication, where as rest three patients had mild intoxication ($< 10\text{ml}$). Most common symptom was

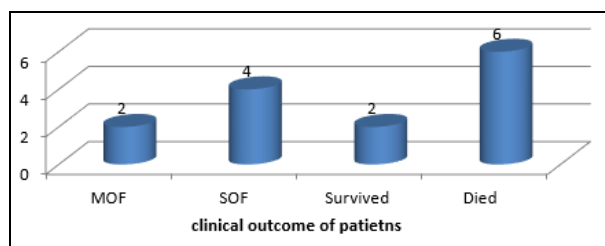
pain in throat and burning sensation followed by vomiting as shown in (table1). In all five cases of severe intoxication, onset of symptoms was immediate and presented with pain in throat and burning sensation, followed by vomiting. Eventually developed pulmonary complications and/or acute renal failure (ARF), and died. Two cases presented with multiorgan failure in few days and died within a week.

Case seven who was 22 year old girl with mild to moderate intoxication (15-20ml) had an unusual presentation. After consuming poison, she did not have any symptoms except for mild burning sensation in throat for next three days until on 4th day she had one episode of vomiting and severe pain in throat after which she revealed history of consuming poison to her parents. Patient was hospitalised elsewhere and then referred to our hospital on 8th day after consumption of poison. During her hospital stay she developed pain abdomen and started having difficulty in breathing. Upper GI endoscopy showed ulceration in stomach, oesophageal and oral mucosa. She was put on ventilatory support. After having initial recovery in second week, she again worsened possibly due lung fibrosis and died on 26th day of admission. Three cases with mild intoxication had minimal symptoms like burning pain in throat and mild difficulty in breathing. These patients survived with complete recovery.

Table 1. Showing presentation and final outcome of paraquat poisoning of patients.

Serial no	Age	Gender	Amount of poison consumed	Presentation on first day	Complication	Outcome
1	24	female	30ml	Throat pain, vomiting, breathlessness	Respiratory failure on 2 nd day	Died on 9 th day
2	22	female	25ml	Burning sensation in throat and pain abdomen.	Respiratory failure on 2 nd day	Died on 10 th day
3	30	Male	40ml	Throat pain, vomiting, breathlessness	Respiratory & renal failure (MOD)	Died within week. 5 th day
4	35	Male	70ml	Throat pain, vomiting, Breathlessness	Multiorgan failure on first day (within 18 hours of ingestion)	Died on 2 nd days
5	26	female	8ml	Vomiting, throat pain and pain abdomen	Respiratory failure 3 rd Day	Died on 9 th day
6	38	female	Less than One teaspoon	Throat pain, difficulty in swallowing, vomiting	----	Survived
7	22	Female	15ml	Mild Burning sensation in throat	Respiratory failure 5 th - 7 th day	Died after 26 th day
8	27	Female	5ml	Throat pain, vomiting	----	Survived

In all eight cases, Pulse, Airway, Breathing and Circulation were initially stabilized and routine oxygen supplementation was avoided due to redox cycling and generation of free radicals[4]. Administration of activated charcoal (1 gm/kg) was given in selective cases who presented to us in first four hours of poisoning. Methylprednisolone, (15 mg/kg body weight) for three days was given in an attempt to suppress the inflammation, followed by maintenance therapy with Hydrocortisone or oral Prednisolone (1mg/kg/day) for at least one month or until recovery or death. Haemodialysis was done in all those cases who presented with renal failure or multi organ failure. Patients were managed with supportive treatment, prophylactic parental antibiotics to prevent secondary infection. We found that cases with severe lung injury or multiorgan failure were associated with high morbidity and mortality. Three cases who survived were followed upto 3months should no signs or symptoms of parkinsonism's.



Graph 1. showing morbidity & mortality in patients with paraquat poisoning

MOF= multiple organ failure , SOF =single organ failure .

DICUSSION

Paraquat is a non-selective contact herbicide, is available in a 20% solution form, widely used in many countries and is highly toxic to humans at a dose of 3–6 g. Symptoms depend upon route of intoxication and are usually dose-dependent. Intoxication can be categorized to mild, moderate, and fulminant. Mild poisoning usually results in full recovery; moderate-to-severe poisoning is fatal in the majority of cases [6]. After oral ingestion, the intestinal absorption of paraquat is poor (1-5%), but still sufficient to elicit a severe and potentially fatal intoxication. Early toxicity includes oral, pharyngeal and gastrointestinal ulcerations and necroses, acute kidney injury and liver failure[7]. Irrespective of its route of administration, paraquat is rapidly distributed in most tissues, with the highest concentration found in lungs and kidneys.

Excretion of paraquat, in its unchanged form, is biphasic, occurs largely in the urine and to a limited extent in bile [8]. The hallmark target of paraquat toxicity is the lung, where available oxygen reacts with

paraquat to produce free radicals. Lung injury undergoes a biphasic response; a) pneumocytes concentrate the compound through active transport, which leads to direct destruction of alveolar epithelium (b) progressive inflammation and proliferation of fibrous tissue produce widespread pulmonary fibrosis [9]. Pneumothorax and pneumomediastinum may result from corrosive injury to the oesophagus [10]. Systemic effects of paraquat are renal and hepatic failure, cardiac failure, shock, and multiorgan failure. Necrosis of proximal tubular cells causes kidney injury, but renal failure is sometimes reversible with aggressive hydration. Treatment involves removal of ingested paraquat by immediate gastric lavage and three to four doses of 60 gm of activated charcoal by gastric tube every two hours. It is only effective if initiated within 4 hours of ingestion, as peak paraquat concentration in the lung is achieved in 5–7 hours [11]. Oxygen as a part of treatment is avoided, because oxygen can rapidly promote generation of free radicals through oxidation. Hemodialysis is used as supportive measure in acute renal failure, but it does not increase clearance of the substance as it is rapidly distributed to the lungs and other organs [12]. Hemoperfusion has often been indicated as an appropriate step of treatment [12] and is considered 4–6 times more effective than hemodialysis [13]. The commonly used drugs include vitamin C, vitamin E, ambroxol, glutathione, and *n*-acetylcysteine. Unfortunately, none of the studied treatments has been proven to be effective [14]. Currently, many experts point out that therapy combining glucocorticoid and cyclophosphamide should be effective to treat PQ poisoning. However, limited evidence exists regarding the appropriate therapeutic dose and duration of treatment [15]. Potent analgesics such as opiates may be required to alleviate intense pain from gastrointestinal tract injury, ulceration, and inflammation. Lung transplantation after paraquat ingestion has been described in case reports[16].

CONCLUSION

This paper highlights two important things, first the mortality rate is very high of around 70% to 80%, with cause of death being hypoxemia, secondary to lung fibrosis. Second that the presentation may be variable and sometimes patients may remain asymptomatic for first few days. Death may occur up to 30 days of ingestion, so patients should be kept under observation even if they are asymptomatic or minimally symptomatic. Aggressive treatment approach should be used before complications will occur. Prognosis of paraquat poisoning is largely dependent on the amount of paraquat ingested.

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