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RESEARCH ARTICLE

ACUTE TOXIN ASSOCIATED KIDNEY INJURY WITH RENAL RECOVERY

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ABSTRACT

Paraquat(1, 1'-dimethyl-4,4'-bipyridium dichloride)is a commonly used contact herbicide in India. Chronic toxicities are not known since it inactivates on coming in contact with soil. The notoriety associated with paraquat is because it came to be used as a commonly used and cheap modality for intentional suicidal use. When ingested, paraquat is quickly but incompletely absorbed and the rest is largely excreted by the kidneys, unchanged, in about 12-24 hours from ingestion. But within the first few hours of ingestion paraquat is actively taken up against a marked concentration gradient into the type II pneumocyte from where the elimination is much slower. Due to its pharmacokinetics, the first two target organs are lungs and kidneys. Suicidal poisoning with paraquat has a very high fatality since there is no known antidote. We present a young lady who presented with a delayed presentation of intentional paraquat poisoning with good renal recovery. The patient however succumbed due to respiratory failure.

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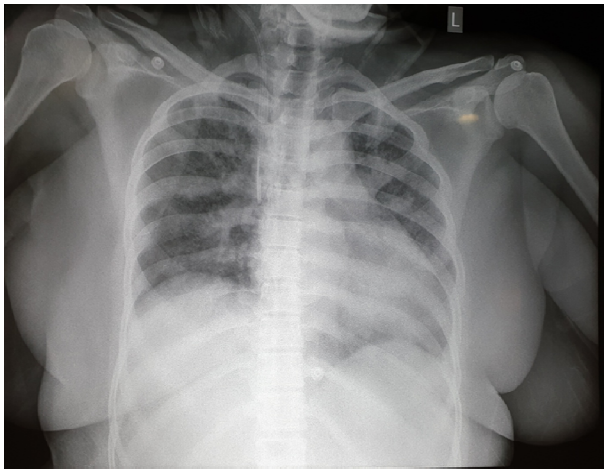
INTRODUCTION

Paraquat is a classified as a bipyridyl compound and has been used widely as herbicide since 1955. Self poisoning with paraquat is a major public health issue in the developing world and also is common in India. While organophosphate poisoning accounts for a majority of self poisoning, paraquat also accounts for a sizable number of deaths due to its very high case fatality rates. Earlier in the 1950-1960s 60-76% of suicidal deaths in England and Wales were attributable to paraquat consumption (Casey, 1994). It was also responsible for more deaths than any other pesticide in the US in their 2008 Data reprt of the American Association of Poison Control (Bronstein, 2008). There are several studies which have looked at paraquat poisoning and their outcomes from the Indian subcontinent (Sandhu, 2003; Saravu *et al*., 2013; Malleshappa, 2013; Jagadeseshan *et al*., 2017; Singh, 1999) The very high case fatality of paraquatof 60-80% is both due to its inherent toxicity and the lack of effective treatment. A paraquat dose of 30mg/kg may be fatal, which is equivalent to 8-10 ml of the 20% solution sold commercially (Yang *et al*., 2012) The prognosis of paraquat poisoning depends on the amount of herbicide consumed. High dose ingestion proves to be fatal in most cases with deaths resulting from multiple organ failure from within hours of ingestion to days. In this case report we present a case of suicidal ingestion of paraquat in a middle-aged female.

Case Report: A 46 year old female was brought to the emergency room by her family with alleged history of ingestion of unknown quantity of paraquat (1, r-dimethyl-4,4'-bipyridium dichloride) in liquid form 6 days back during an alleged suicide attempt. The patient was previously diagnosed to have severe depression, though she did not have any h/o suicidal attempts in the past. She also did not notify anyone till 5 days after ingestion. Upon notification, she was initially treated at a local hospital with intravenous fluids and referred to our hospital due to deranged renal and hepatic functions. There was no history of nausea, vomiting, loose stools, seizures or altered bowel or bladder habits. Oral examination showed lesions that are consistent with ulceration secondary to paraquat (Fig 1). On presentation, the pulse rate was 102 beats per minute and regular, BP was 126/80 mmhg on right arm supine position, respiratory rate of 22 cycles per minute and SpO_2 of 96% on room air. The respiratory and cardiovascular systems were normal on examination.



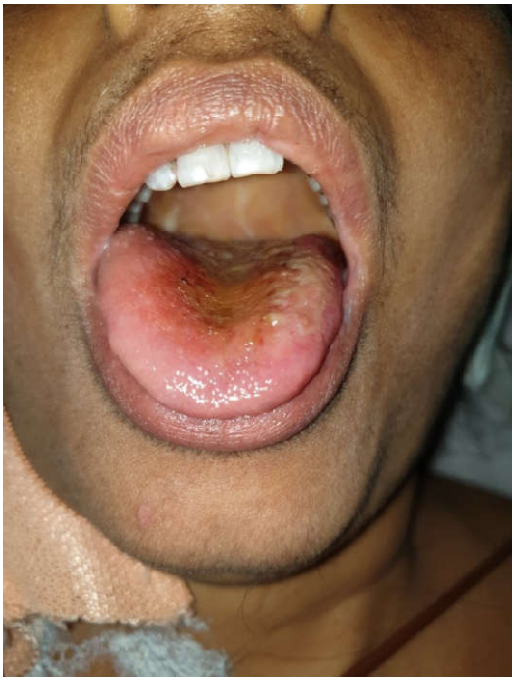


Table 1. Laboratory investigations of the patient .

Investigations	Day 1	Day 4	Day 7	Day 10
Urea (mg/dL)	202.4	90.9	99.6	80.5
Creatinine (mg/dL)	11.23	2.17	1.22	1.14
SGOT (IU/L)	300	202	93	83
SGPT (IU/L)	368	385	320	282
ALP (IU/L)	300	344	365	483

She was admitted in the intensive care unit for observation. Her chest Xray appeared to be normal on admission (Fig 2) and ECG did not show any acute changes. On admission, she was found to have a blood urea of 202.4 mg/dL and a creatinine of 11.23 mg/dL. Relevant investigations are shown in Table 1.She underwent emergency haemodialysis on the day of admission followed by 2 more cycles of haemodialysis after which the renal functions stabilised. The patient was non oliguric throughout and urine routine evaluation was found to be normal. Ultrasound of the abdomen showed normal sized kidneys with bilateral grade I renal parenchymal changes.Her total leucocyte count was 13,500 cells/cumm which climbed up to 21,300 cells/cumm. Her liver functions were also found to be deranged with Total bilirubin of 4.33mg/dL (direct 3.93 and indirect 1.0) SGOT 300 U/L, SGPT 368 U/L and ALP 300 U/L. Two-dimensional (2D) Echocardiogram was found to be normal. During the course of hospital stay, her renal and liver functions improved but the patient went into type 1 respiratory failure after 2 days of hospitalisation and patient was initiated on non-invasive ventilation. She was treated with IV fluids, high dose IV dexamethasone and IV antibiotics. Patient died subsequent to acute respiratory distress syndrome (ARDS)after one week in the ICU despite good liver cell and renal recovery.

DISCUSSION

Paraquat is highly toxic to humans and the toxicity is a manifestation of its ability to undergo redox□cycling and subsequent generation of reactive oxygen species (ROS) (Yang *et al*., 2012). These effects are responsible for lipid peroxidation and cell death. A second contributing factor for toxicity is the depletion of nicotinamide adenine dinucleotide phosphate with bound hydrogen ion (NADPH), as both paraquat redox cycling as well as hydrogen peroxide detoxification is NADPH dependent. The clinical course depends on the amount ingested. The volume of distribution of paraquat is 1-2L/kg and it is unbound to plasma proteins. Plasma paraquat concentration exhibits a mean half –life of 5 hrs and a mean elimination half-life of 84hrs (Houze *et al*., 1990). After ingestion, the greatest levels are fond in the lungs with peak concentration in 5-7 hrs (Bismuth *et al*., 1990). Selective accumulation in the lungs leads to capillary endothelial and epithelial cell injury leading to diffuse alveloitis and ultimately pulmonary fibrosis in survivors. Gastrointestinal toxicity is a universal feature and erosion of the oral mucosa is found even in patients who spit out the poison without ingestion. In patients where the poisoning results in death, it is mostly caused due to pulmonary congestion followed by pulmonary haemorrhage and pulmonary fibrosis (Drechsel, 2009). It causes diffuse alveolar collapse, vascular congestion and adherence of activated platelets and polymorphonuclear leucocytes to the vascular endothelium. It is also responsible for apoptosis of cells in the lungs. Paraquat is eliminated mainly by the kidney and acute kidney failure is a recognised complication with reports of nonoliguric and oliguric cases (Sobha *et al*., 1989; Bullivant, 1966).

Proximal tubular necrosis by histopathological examination in a fatal case was found by Beebeejaun (Beebeejaun, 1971) and this is consistent with renal tubular toxicity found in mice. Paraquat poisoning may lead to a Fanconi syndrome with proximal tubular abnormalities including glycosuria, phosphaturia and aminoaciduria as shown in a series of 3 cases reported by Vaziri *et al*. (1979). Patients who present with features of systemic toxicity within the first 24 hours of presentation (e.g. hypotension, severe hypoxia, acidosis and low GCS) have extremely poor prognosis. The development of renal failure, changes on chest X-ray and extensive gastrointestinal lesions are all adverse prognostic signs (Vale, 1987). In patients with higher concentrations of paraquat in urine, the colour changes to blue which indicates grave prognosis (Smith, 1974). The current treatment modalities available are limited in view of lack of a specific antidote. Gastric lavage with 1% bentonite solution has been found to prevent gastrointestinal contamination for patients who present within one hour of ingestion and activated charcoal was found to be effective in lowering serum paraquat levels when given after more than one hour of ingestion (Idid, 1996). Paraquat is not removed by hemodialysis and is of little use due to the rapid absorption and clearance of the toxin from the body. Besides, by the time haemodialysis is initiated the toxin is

absorbed by the lung creating an extra compartment from where elimination via haemodialysis is difficult. That said, haemodialysis is still beneficial in patients who develop acute renal failure (Dinis□Oliveira *et al*., 2007). In spite of undergoing haemodialysis in such patients the prognosis remains poor due to irreversible lung injury. Renal recovery though has been described infrequently (Ali, 2016).

The other treatment modality used currently is immunosuppression with either dexamethasone or cyclophosphamide. The rationale behind this is to prevent inflammatory lung injury. But in spite of advances in treatment, the case fatality remains high in patients with ingestion of large amounts of toxin attributable to multi-organ failure and quick setting in of respiratory failure. Late referral to hospital, severity of poisoning and multiorgan failure are the main causes for increased mortality (Malleshappa, 2013). Our patient presented to us five days after alleged consumption of paraquat and had both hepatic and renal toxicity at admission. She received high dose dexamethasone therapy and hemodialysis along with supportive care. We did not facilities for estimating serum paraquat levels or hemoperfusion at our centre.Lung toxicity developed as a delayed complication and ultimately lead to her demise.

Conclusion

Paraquat consumption is a rare agent for suicidal poisoning and results in very high mortality and morbidity. There is no specific antidote for paraquat poisoning and treatment is largely supportive. Acute kidney injury is recognised complication and needs immediate treatment. In view of its use as suicidal agent, its use and administration needs stricter control.

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