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Original Research Article

Clinical spectrum and outcome of paraquat poisoning in a tertiary care teaching hospital

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ABSTRACT

Background: Paraquat is most common insecticide compound used for suicidal consumption in rural part of the Karnataka next to organo-phosphorous compound. It produces various local and systemic manifestations in the early course. It is very notorious to cause multi-organ dysfunction and mortality within 24 hours in severe amount of consumption. Lack of specific antidote and high-quality evidence-based medicine makes the management of paraquat poisoning challenging. Hence, we took up the study to evaluate the clinical features, course and management option for the poisoning.
Methods: It is an observational study conducted at HIMS, Hassan. History was collected from patient and bystanders. Clinical features, laboratory parameters were noted regularly and frequently. Patient's complications were identified initially and treated accordingly. All the data collected were tabulated and statistically analysed.
Results: Out of 110 patients, 72 were females and 38 were males; most of them were in the age group of 30-40 years. Mild poisoning was noted in 30, moderate in 56 and 24 patients were severe. Most common symptom was nausea and signs were oral cavity ulcers followed by tachycardia and tachypnoea. The overall mortality was 72%, 18% were recovered fully and 10% patients left against medical advice.
Conclusions: Since there is a lack of antidote management of paraquat is challenging. Early gastric lavage, aggressive fluids, IV methyl prednisolone and N-Acetyl-Cysteine is beneficial.

Keywords: Acute renal failure, Free radicals, Multi-organ dysfunction, Paraquat, pulmonary fibrosis

INTRODUCTION

Paraquat is a pungent smelling, synthetic, non-selective contact herbicide. It is available as 20% solution that needs to be diluted before agricultural use. When toxic dose is ingested it produces various local manifestations and life threatening systemic manifestations involving gastro-intestinal tract, cardiovascular system, respiratory system and renal system. The lethal dose (LD50) for humans is 3-5 mg/kg that is as little as 15-20 ml of 20% solution.[1] This compound is very frequently used in this part of the state and it carries high mortality. Since there is a lack of specific antidote and lack of high quality evidence-based medicine for the management of the poison, we have taken up this study to identify the various clinical features, course and to evaluate the best therapeutic options for the management of patient with paraquat consumption.

METHODS

The study was a retrospective analysis of first 23 consecutive cases operated by the first author between July 2012 and July 2014. All patients were preoperatively evaluated clinically and radiologically. In infants and children, increasing head circumference, tense and

bulging anterior fontanelle, Sun set sign (downward fixed gaze), failure to thrive, poor feeding and delayed/ regression of milestones were considered as the positive clinical findings.

Altered sensorium, progressive neurological deficits, late onset seizures, features of raised intracranial pressure with or without headache and vomiting were considered as positive findings in adults.

RESULTS

Out of 110 patients, 72 (66%) were females and 38 (44%) were males (Graph 1); most of them were in the age group of 30-40 years (Table 1).

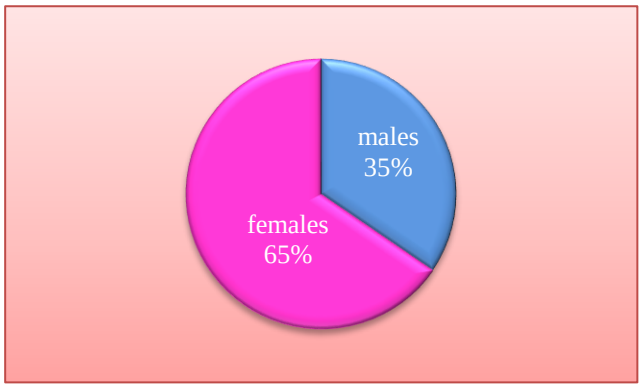

Figure 1: Sex-wise distribution of the sample size involved in the study.

Table 1: Age wise distribution of the patients involved in the study.

Age group	Sample size
<20	01
21-30	23
31-40	70
41-50	10
51-60	06

Mild poisoning was noted in 30 (28%) patients, moderate in 56 (51%) patients and 24 (21%) patients were severe. Severity of the poison is given in Figure 2 and mode of poisoning given in Figure 3.

Most common symptom was nausea observed in all patients followed by throat pain and cough. Most common sign was oral cavity ulcers followed by tachycardia and tachypnoea (Table 2).

Most common organ complication noted was acute renal failure; observed in 85 (77%), followed by hepatic dysfunction in 65 (59%) patients, respiratory failure observed in 54 (49%) patients and multi organ dysfunction in 50 (46%) patients. The mean creatinine value was 4.2 mg% in patients who developed acute renal failure. Out of 85 patients, 60 patients underwent haemodialysis. The indications for dialysis were symptoms of uraemia, acidosis and hyperkalaemia.

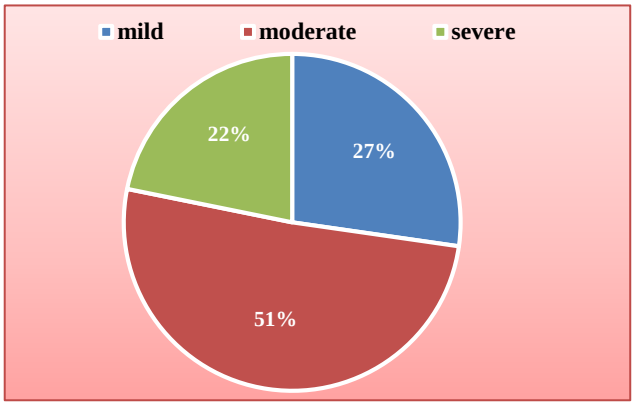

Figure 2: Distribution of the sample based on the severity of the poisoning.

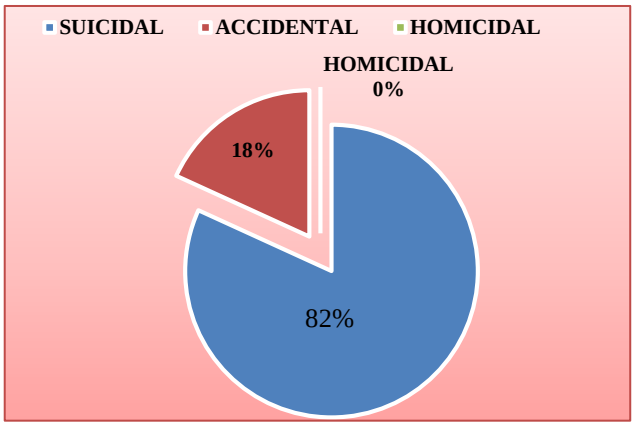

Figure 3: Distribution of the patients based on the mode of ingestion of the poison.

The outcome of the poisoning was given in Graph 4. The overall mortality was 72% (80 patients), 18% (20 patients) were recovered fully and 10 (10%) patients left against medical advice.

Mean duration of death was 12 days, 8 patients died within 24 hours of hospitalization. Common cause of death was multiorgan dysfunction.

Table 2: Clinical features of the paraquat poison in study population.

Symptoms	%	Sign	%
Nausea	100	Oral ulcers	95
Throat pain	94	Tachypnea	90
Cough	85	Tachycardia	90
Vomiting	70	Hypoxia	85
Headache	70	Icterus	80
Abdominal pain	68	Hypotension	80
Chest pain	58		
Loose stools	16		
Breathlessness	60		

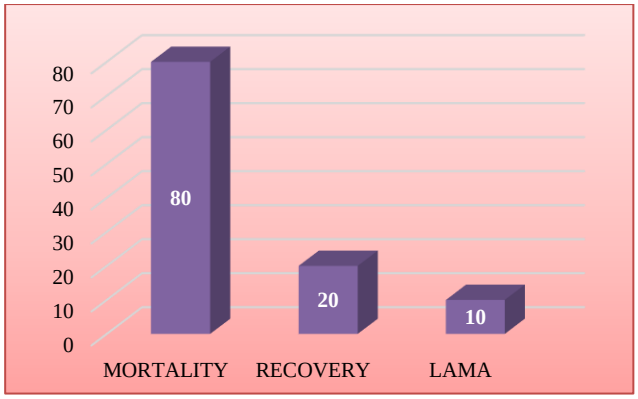

Figure 4: Outcome of the poisoning.

DISCUSSION

It is produced commercially as a brownish concentrated liquid of the dichloride salt in 20% strength under the trade name of "Gramoxone®" and for horticultural use as brown granules called "Weedol®" (Syngenta India Limited, Plot No B-155/1, Bharuch, Gujarat, India) about 5% concentration.[2]

Route of poisoning are inhalation, contact and ingestion, later being the most common route of poisoning. Ingestion of paraquat results in local ulceration and rapid absorption into systemic circulation. Inhalation results in local irritation. Dermal manifestations though rare, have been noted in severe poisoning.

Paraquat is rapidly but incompletely absorbed, not actively metabolized and more than 90% is excreted unchanged by the kidneys. After absorption, it is distributed to highly perfused organs like lungs, kidneys, liver, and muscles, and remains partly in the intravascular space.

Paraquat concentration in the lung parenchyma is very high because of active, energy-dependent uptake of paraquat by type 1 and type 2 alveolar epithelium, via the polyamine uptake pathway.[3]

Paraquat, during "redox-cycling-process" leads to the formation of superoxide anions from which more toxic reactive oxygen species (ROS) such as hydrogen peroxide and hydroxyl radicle are formed in the presence of NADPH and cytochrome P450 reductase.[4]

If the protective mechanisms such as catalase and glutathione peroxidase are overwhelmed, the resultant oxidative stress will cause cellular damage.

The hydroxyl radical, which is formed in the presence of iron, is a more potent oxidant and can induce lipid peroxidation which causes cell membrane damage and cell death.[5] The clinical manifestations range from local irritation to multiple-organ failure and death. Systemic manifestations depend on the amount ingested, and patients can be classified into 3 categories (Table 3).[6]

Table 3: Clinical features of the poisoning.

Clinical features of the poisoning	
Mild poisoning	These patients may have gastrointestinal symptoms but usually fully recover
Moderate poisoning	Severe caustic lesions in the gastrointestinal tract
	Acute renal failure
	Progressive pulmonary fibrosis
	Deaths occur in 2-3 weeks, from severe respiratory failure
Severe poisoning	Multiple-organ failure leading to death within hours to a few days after ingestion

The diagnosis is usually from the accurate history of exposure from the bystanders, verification of the container brought by the patient or bystanders.

This can be difficult in children and case of homicide.[7] The urine dithionite test quickly confirms the presence of paraquat in urine. A paraquat blood level of >1.6 µg/mL 12 h after ingestion is universally lethal. [8]

Initial management focuses on prevention of further absorption and gastrointestinal decontamination. Adsorbents like activated charcoal (1-2 g/kg) and Fuller's earth (1-2 g/kg); given with a cathartic such as 70% sorbitol should be given as soon as possible. There is no specific antidote. Paraquat is not removed by dialysis. Hemodialysis is used only as a supportive treatment for patients who develop kidney failure.[9]

In a study by Afzali et al., the therapeutic effect has been reported with high dose cyclophosphamide and glucocorticoid where survival was about 75%.[10] This was further supported by Agarwal et al. Since there is a lack of clear evidence-based therapy, different approaches have been tried for supportive management.[11,12]

Although high doses of cyclophosphamide and Dexamethasone treatments, including intravenous cyclophosphamide (5 mg/kg/d) and dexamethasone (24 mg/d) for 14 days have been correlated with 75% survival rate after poisoning,[13] a subsequent study did not demonstrate the usefulness of this approach.[14]

A report demonstrated that pulse therapy with cyclophosphamide and methyl prednisolone (MP) might be effective in preventing respiratory failure and reducing mortality in patients with moderate to severe poisoning.[15] Pulse therapy with MP is known as a strong anti-inflammatory treatment in clinical practice, suppressing ROS production by neutrophils and macrophages, and in the arachidonic acid cascade.[16,17]

It has been shown that desferrioxamine can exert its protective effects not only by iron chelating but also by blocking the uptake of paraquat by the alveolar type II cells.[18]

Vitamin E (a-tocopherol) exerts its antioxidant effects by scavenging free radicals and stabilizing membranes containing polyunsaturated fatty acids, which may prevent the cytotoxic effects of paraquat.[19]

N-acetyl cysteine has also been used with success in severe paraquat poisoning.[20] It is an excellent source of sulfhydryl groups. NAC is indeed converted in the body into cysteine, the rate-limiting amino acid for glutathione synthesis, promoting detoxification, and acting directly as a free radical scavenger.[21]

Other supportive care includes fluid and electrolyte management and pain control. Oxygen supplementation should be avoided if possible because it can potentiate paraquat induced lung injury.

Oxygen is indicated when patient develops hypoxia. Limitations in the management are, not used all the treatment plans discussed above. Since there is no evidence based standard protocol, and lack of specific antidote makes the management of paraquat poisoning difficult.

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