Original Article

Clinico-epidemiological Profile of Paraquat Poisoning in Children at a Tertiary Care Centre: Case Series

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Abstract

Aims and objectives: This case series is done to know the Clinico-epidemiological profile of paraquat poisoning in children and also the implication of available treatment guidelines in improving outcomes in the paediatric population as there are no standard treatment guidelines available.

Materials and Methods: Nine children were selected during the study period of October 2021 to February 2023, demographic data were collected, clinical parameters were assessed with details such as time of presentation, symptoms and first aid received, laboratory parameters such as LFT, RFT, chest radiographs obtained and serial values monitored. Treatment as per the available recommendation was initiated with immunosuppressive therapy and haemodialysis on a case-to-case basis.

Results: Among the 9 children, there were 6 females (67%) with an average age group of 15–18 years. eight (89%) of the 9 children developed acute renal failure. Seven children underwent haemodialysis. Five (55%) children developed hepatic dysfunction. Among the 9 children, 3 (67%) survived.

Conclusion: The study reveals that the mortality rate can be reduced, if the child presented to the hospital within 8 hours of ingestion of the compound, amount ingested is less than 20 ml, and early initiation of Haemodialysis within 8 hours and a trail of immunosuppressive therapy.

Keywords: Paraquat poisoning, haemodialysis, immunosuppressive therapy

Introduction

Paraquat is a commonly used herbicide in India. Suicides due to paraquat (PQ) are an important cause of morbidity and mortality because there is no specific antidote available. The chemical structure of paraquat is 1,1′-dimethyl-4,4′-bipyridinium. It belongs to the group of dipyridyl herbicides[1]. Paraquat was first manufactured as a nonselective, quick-acting pesticide by a British chemical company in 1962. It was rapidly absorbed by the plants and inactivated in contact with clay in the soil, leaving minimal residue. It is extremely toxic to humans, and even minimal ingestion of 10–20 mL of 20% paraquat is lethal[2] and can lead to renal failure, hepatotoxicity, and pulmonary fibrosis. The case fatality rate in paraquat is as high as 70%.

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Paraquat poisoning can be classified into 3 categories [2]

Mild/subacute poisoning - <20 mg/kg body weight

Moderate/severe acute poisoning - 20–40 mg/kg body weight

Fulminant/hyperacute poisoning >40 mg/kg body weight.

The use of immunosuppressive therapy (a combination of glucocorticoids and cyclophosphamide) may be beneficial in improving survival in these patients [3,4].

Paraquat poisoning in children is very rare, there are no case studies available for paraquat poisoning in children and no standard treatment guidelines for managing such cases are available. We report our experience of treating nine children of paraquat poisoning with immunosuppressive therapy and other supportive measures at Hassan institute of medical sciences, Karnataka.

Methodology

All the children who presented with an alleged history of paraquat consumption were included in the study, a total of nine children over a period of 2 years (October 2021- February 2023) were taken into the study. The bio-data with age, sex, time of consumption, symptoms, first aid received, and treatment given were collected. Informed consent was taken. Laboratory parameters such as renal function test, liver function test, and chest radiographs were obtained. Serial values were monitored and assessed. Paraquat levels could not be assessed due to the non-availability of investigations required. The data was collected in a predetermined proforma sheet. Data were analysed in a descriptive pattern.

Following complications were monitored. Children were classified to have renal dysfunction according to the eGFR. Calculation of eGFR was done based on the Schwartz formula (eGFR = 0.55 × Height/Creatinine) [5]. Renal failure was classified based on acute kidney injury classification using pRIFLE criteria (table 1) and serial creatinine values was monitored.

Table 1: pRIFLE criteria.

Staging	Serum creatinine criteria	Urine output criteria
Risk	eGFR decreased by ≥25%	0.5 mL/kg/hr for 8 hr
Injury	eGFR decreased by ≥50%	0.5 mL/kg/hr for 16 hr
Failure	eGFR decreased by ≥75% or <35 mL/min/1.73 m2	0.3 mL/kg/hr for 24 hr or anuria for 12 hr
Loss	Persistent failure >4 weeks	
ESRD	Persistent failure >3 months	

eGFR, estimated glomerular filtration rate; ESRD, end-stage renal disease

Hepatic dysfunction was considered if serum bilirubin was > 2mg/dL. Children were monitored for signs of acute lung injury, acute respiratory failure, and circulatory failure.

Children were treated with the following medications, as per the available recommendations.

1. Airway, breathing and circulatory support
2. Gastric lavage and decontamination by activated charcoal
3. Skin and eye decontamination
4. Enhance elimination – haemodialysis
5. IV antibiotics – Amoxiclav 50mg/kg/day in 2 divided doses to prevent infection
6. Antioxidant therapy - Vitamin C (500mg/tab) once a day.

   Vitamin E (400 IU/ tab) once a day.

   Intravenous N-Acetyl cysteine 2g/day for 3 days.
7. Intravenous Methylprednisolone 30 mg/kg/day for three consecutive days.
8. Intravenous Cyclophosphamide 15 mg/kg/day for two consecutive days, followed by Intravenous Dexamethasone 8mg thrice a day until recovery or death.

Results and Analysis

The nine children treated for paraquat poisoning are summarised in table 2.

Table 2: Case summary of paraquat poisoning

CASES	1	2	3	4	5	6	7	8	9
Age/Sex	**13y/M**	**16y/F**	**15y/M**	**16y/F**	**16y/M**	**16y/F**	**17y/M**	**16y/F**	**17y/F**
Time of presentation	2 hours	10 hrs	2 hrs	4 hours	5 hours	3 hours	3 hrs	3 hrs	3 hours
Amount	2-5 ml	50 ml	30-40 ml	5 ml	50-60 ml	40-50 ml	40-50 ml	~50 ml	10-20 ml
Complications	Nil	ARF, ALI,	ARF, ALI, PF	ARF	ARF, ALI,	ARF, ALI, with shock	ARF, ALI,	ARF, ALI, PF	ARF, PF
Peak Serum Creatinine (mg/dL)	0.75	5.07	4.98	4.2	6.09	2.3	3.21	2.96	2.99
Lowest eGFR (ml/kg/1.73m^2)	102	15.9	17.4	20.9	14.4	40.6	24.5	26.7	29.9
Peak serum bilirubin (mg/dL)	0.6	3.3	26.3	2.3	4.3	0.8	0.7	8.1	0.7
Treatment	GL, AOT	GL, AOT	GL, HD, AOT	GL, HD, AOT	GL, HD, AOT	GL, HD, AOT	GL, HD, AOT, IST	GL, HD, AOT, IST	GL, HD, AOT, IST
Haemodialysis	Nil	Nil	7 cycles	1 cycle	3 cycles	2 cycles	2 cycles	5 cycles	7 cycles
Time of initiation of HD	NA	NA	22 hours	16 hours	20 hours	24 hours	12 hours	8 hours	8 hours
Ventilation	NA	MV	MV	NA	MV	MV	MV	MV	Oxygen
ICU stay	2 days	8 hours	11 days	2 days	2 days	3 days	2 days	8 days	7 days
Outcome	Survival	Death (8hrs)	Death (11 days)	Survival	Death (30hrs)	Death (48hrs)	Death (43hrs)	Death (8 days)	Survival

AOT: antioxidant therapies; ARF: acute renal failure; ALI: acute liver injury; Cr: creatinine; F: female; GL: gastric lavage; HD: haemodialysis; M: male; MV: mechanical ventilation; NA: not applicable; NIV: non-invasive ventilation; PF: pulmonary fibrosis; IST: Immunosuppressive therapy.

The children were in the age group of 15-18 years, among the nine children, six were females (67%) and 3 males (33%), figure 1. Eight children presented to the hospital within 3 hours of ingestion, figure 2. On monitoring of the above children, eight (89%) of nine cases developed acute renal failure with a peak serum creatinine of 6.09mg/dL, and eGFR 14.4ml/kg/1.73m^2, figure 3. Seven children underwent haemodialysis, of which, two children (33%) underwent haemodialysis within 8 hours, one (16.6%) child within 12 hours, and four (67%) of them within 24 hours of ingestion of the compound.

Among the nine children, five (55.5%) developed hepatic dysfunction with peak serum total bilirubin of 26.3 mg/dL, of which serum indirect bilirubin was 15mg/dL.

Seven(78%) children developed respiratory distress, of which 6 received NIV and mechanical ventilation, and one child received oxygen therapy.

One child developed circulatory failure and shock.

Among the 9 children, 3 (33%) survived, figure 4,

Case No.1, the first case of survival, presented within 2 hours of consumption, had consumed a very small amount of the compound and did not develop any renal and liver dysfunction or respiratory compromise.

Case No. 4, the second case of survival presented within 3 hours of consumption, child was initiated with gastric lavage, and antioxidant therapy, had normal creatinine and eGFR on admission, underwent haemodialysis within 12 hours of consumption, started developing raising titres of serum creatinine, peak serum creatinine being 3.21mg/dL and reduction of eGFR, lowest being 24.5ml/kg/1.73m^2. After 4 cycles of haemodialysis serum creatinine values gradually reduced and improvement in eGFR was noted. There was no hepatic dysfunction or respiratory compromise.

Case No. 9, the third case of survival, presented to the hospital within 3 hours of consumption, initiated with gastric lavage, antioxidant therapy, and immunosuppressive therapy, even though with initial LFT and RFT were normal, the child underwent haemodialysis within 8 hours of consumption. However, the Child developed renal dysfunction with raising creatinine on day 3, peak value being 2.9mg/dL, and the lowest eGFR of 29ml/kg/1.73m^2. The child underwent 7 cycles of haemodialysis, following which creatinine values reached normal after 6 days. The child developed respiratory distress on day 10, chest x-ray suggestive of pulmonary fibrosis, figure 5, the child was continued with minimal oxygen support, antioxidants and immunosuppressants, which improved in a week. The child did not have hepatic dysfunction.

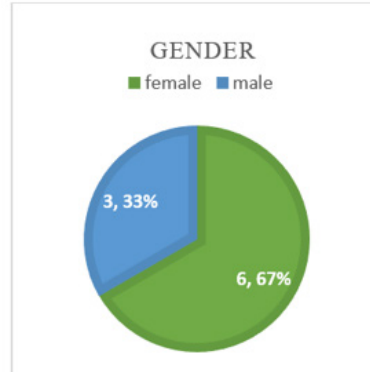

Figure 1: Gender distribution

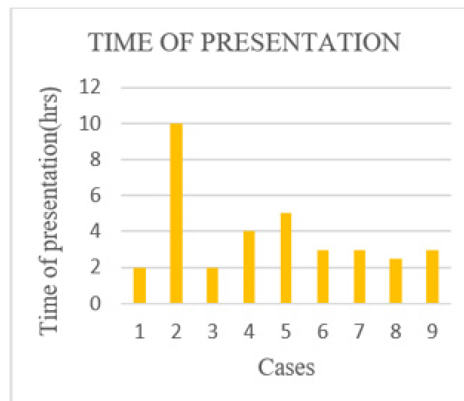

Figure 2: Time of presentation

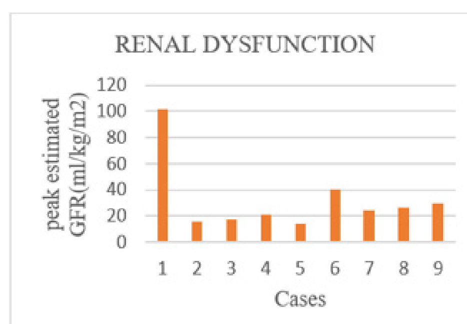

Figure 3: Lowest eGFR

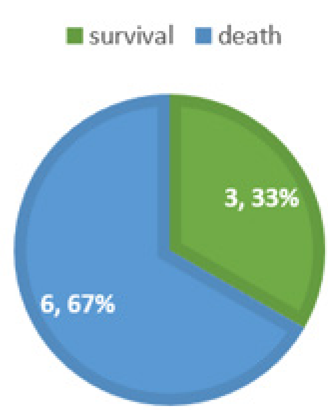

Figure 4: Mortality among the cases

Figure 5: Pulmonary Fibrosis

Discussion

Paraquat was first manufactured and sold in early 1962 under the trade name Gramoxone, and commonly used herbicide. Paraquat is classified as a non-selective contact herbicide. It kills a wide range of annual grasses, broad-leaved weeds, and the tips of established perennial weeds. The principal target organ for paraquat poisoning is the lung and kidney, figure 5. Paraquat-induced toxicity is mainly due to generation of reactive oxygen species (ROS). Due to the uptake of paraquat against the concentration gradient in the lungs, the production of free radicals results in greater toxicity in the lungs as compared to other organs.

Due to the presence of free radicals and reactive oxygen species, lipid peroxidation occurs, leading to cell membrane damage and apoptosis.

Paraquat toxicity is most severe in the lungs and leads to acute alveolitis and diffuse alveolar collapse [6]. During the acute 'destructive phase' both type I and type II pneumocytes demonstrate swelling, vacuolation and disruption of mitochondria and the endoplasmic reticulum. Kidneys exposed to paraquat demonstrate the development of large vacuolation in proximal convoluted tubules which leads to necrosis[7].

Congestion and hepatocellular injury associated with rough and smooth endoplasmic reticulum degranulation and mitochondrial damage occur in the liver.

As of today, paraquat poisoning has no specific antidote, and supportive therapy is the mainstay of treatment for the prevention of lung injury from free radicals. The modalities include steroid pulse therapy (methylprednisolone, dexamethasone) along with cyclophosphamide for preventing the development of pulmonary fibrosis and haemodialysis to aid in eliminating paraquat from the circulation and gastric decontamination. It is important to note however that administering oxygen has been shown to increase paraquat toxicity through the provision of electron acceptors and thus should be used sparingly in those who are hypoxic. Even with aggressive treatment, the mortality in paraquat poisoning is alarmingly high, with the cause being multiorgan dysfunction and respiratory failure. There are a few exceptions with patient survival, but these can be attributed to ingestion of a smaller dose or early initiation of treatment and the outlook for a patient with ingestion of a higher dose or severe paraquat poisoning is still poor. Taking this into consideration, the crux of the management of paraquat poisoning comprises mainly preventive measures and early and aggressive decontamination to prevent any further absorption of the compound.

A case series by Pavan described to have a mortality of 35% to 50% in patients with paraquat poisoning, with all patients developing acute kidney injury, they described respiratory and multiorgan failure as the main causes of mortality.[8]

In a study by Lin et al., a therapeutic effect has been reported with a high dose of cyclophosphamide and glucocorticoid where survival is about 75%.[9] However, in our study, 3 children were initiated with immunosuppressive therapy, among which one child survived (33%).

An intensive care unit study and a meta-analysis conducted by Agarwal et al. concluded that immunosuppressive therapy with cyclophosphamide and glucocorticoids has a potential role in the management of paraquat poisoning in moderate to severe poisoning cases [10,11]

Conclusion and Recommendation

The study reveals that the mortality rate can be reduced, if the child presented to the hospital within

8 hours of ingestion of the compound, the amount ingested is less than 20 ml and early initiation of Haemodialysis within 8 hours and a trial of immunosuppressive therapy.

Case reports on paediatric paraquat poisoning are not available, further studies are required for recommending treatment guidelines, as there is no specific antidote available and the compound is highly toxic, with high mortality rates, we should aim at preventing such exposures, and measures need to be taken to withdraw or limit the use of such compounds.

Limitation of the study:

- Paraquat levels were not measured.
- All children were not initiated with immunosuppressive therapy.

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Conflict of interest: None Declared

Ethical approval: the study was approved by the Institutional Ethics Committee- Hassan Institute of Medical Sciences, Hassan. Date: 07/03/2023, Reference number: IEC/HIMS/RR 396

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