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RESEARCH ARTICLE

A CLINICAL PROFILE OF PARAQUAT POISONING IN A TERTIARY CARE HOSPITAL: A CASE SERIES

[1,*]Krishanko Das, [2]Prof. Shantasil Pain and [3]Prof. Nandini Chatterjee

[1]PGT, Department of Medicine, IPGME & R and SSKM Hospital
[2,3]Professor, Department of Medicine, IPGME&R and SSKM Hospital

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ABSTRACT

Background: Paraquat is a widely used weedicide in India. It is now being increasingly used as a suicidal poisoning and is almost always fatal as there is no specific antidote for paraquat poison. ARDS, acute kidney injury or multi-organ failure are the frequent causes of mortality. **Methods:** The study aimed to study the morbidity and mortality rates of Paraquat poisoning in tertiary care hospital. Patients admitted with Paraquat poisoning were included, and the data collected and analysed. **Results:** The total number of cases admitted with paraquat poisoning in the General Medicine Ward and Intensive Care Unit in nine months duration were 22 out of which 18 were suicidal and 4 were accidental ingestion. 84% of cases died within a week of ingestion. Almost all of them had Acute Kidney Injury and finally succumbed to multi-organ failure. The overall mortality rate was 72% despite best efforts. Higher mortality has been associated with delayed presentation. No correlation was found between higher creatinine values at presentation and outcome. **Conclusions:** Thus, paraquat poisoning is very serious and life threatening. Inspite of supportive haemodialysis, steroids and cyclophosphamide therapy, antibiotics, it was ineffective in reducing the mortality rates. Hemoperfusion if initiated within 4 hours of ingestion showed a better outcome but none of the patient presented to our side within 4 hour of ingestion. Paraquat is now banned in 32 countries but still poses a major threat as a suicidal agent in India.

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INTRODUCTION

Paraquat poisoning is a major health problem worldwide especially in a developing and predominantly agricultural based country like India. Chemically, Paraquat is 1, r-dimethyl-4,4'-bipyridium dichloride, a toxic bipyridyl herbicide, a greenish corrosive liquid with a pungent smell. Its herbicidal properties were discovered in 1950s and first marketed in 1962 (Arts, 2006). It is one of the most widely used herbicides in the world, and in most countries where it is registered it can be used without restriction. Death in paraquat poisoning is either due to significant lung injury, acute kidney injury or multi organ failure. The commonest mode of poisoning with paraquat is self oral intake of poison.

Regulatory Status: The World Health Organisation (WHO) enlists paraquat as a Class II-moderately hazardous pesticide while the Pesticide Action Network (PAN) International has categorized it as a highly hazardous pesticide with high acute toxicity.

Corresponding author:* **Krishanko Das,
PGT, Department of Medicine, IPGME & R and SSKM Hospital.

Paraquat is banned in 32 countries, including the 27 countries of the European Union. Malaysia banned paraquat in 2002, with all use to be phased out by 2005. Paraquat was due to be phased out altogether in Sri Lanka by the end of 2009.

Indian Scenario: Paraquat dichloride (24% SL) is the only formulation iregistered in India with the Central Insecticide Board and Registration Committee (CIBRC). Although CIBRC has not provided any recommendations, it has approved the use of this herbicide in nine crops. Paraquat dimethyl sulfate, another formulation, was banned in India in 1993 (CIBRC 2014).

Paraquat is one of the most frequently used pesticides to commit suicide but surprisingly, there is no antidote for paraquat. The mortality rate for paraquat poisoning is very high, at 42 to 80%. It has been reported from various regions of India ranging from the northern States to the southern States and northeast States (Khosya S and Gothwal S V, 2012; Pavan M, 2013; Narendra S *et al*., 2013; Raina S, 2008; Saravu K *et al*., 2013; Sandhu JS *et al*., 2003; Raghu K *et al*., 2013; Banday T H *et al*., 2014; Khan S U, 1975; Tayade S, 2013; Sarojini T, 2007). Currently, after Kerala Government order in 2011, paraquat is not being used in Kerala.

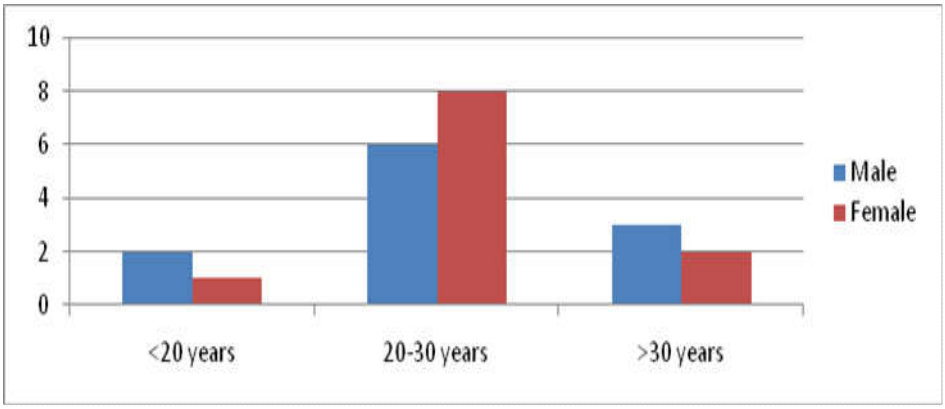
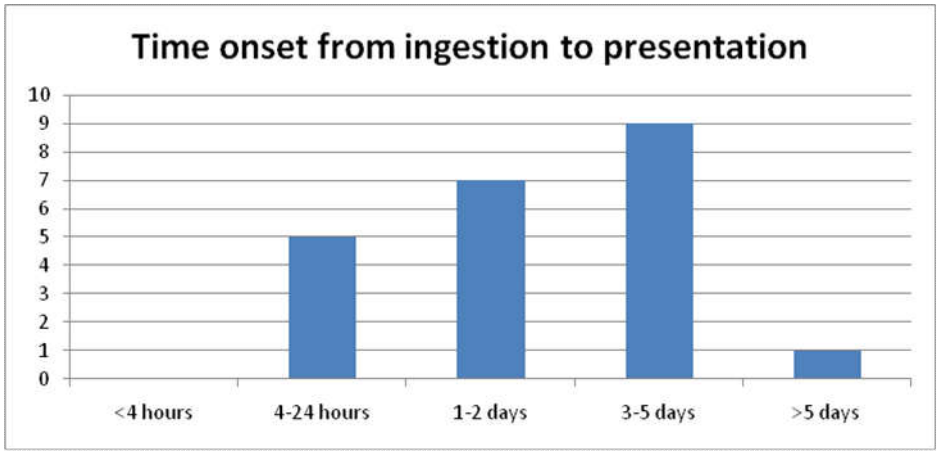


Figure 1. Age and sex distribution of patients presenting with paraquat poisoning (n=22)



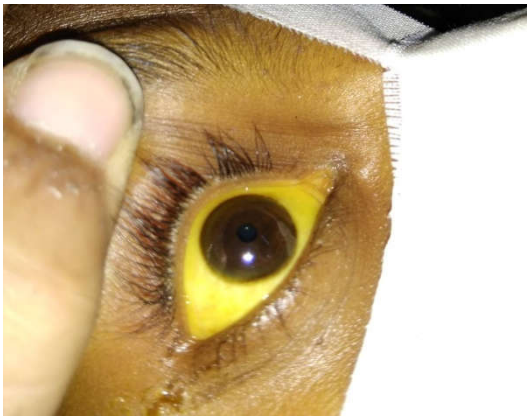


Figure 3. Icterus following paraquat poisoning

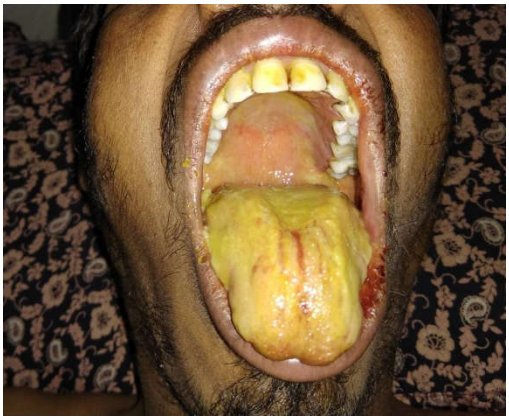


Figure 4. Yellow tongue following paraquat ingestion

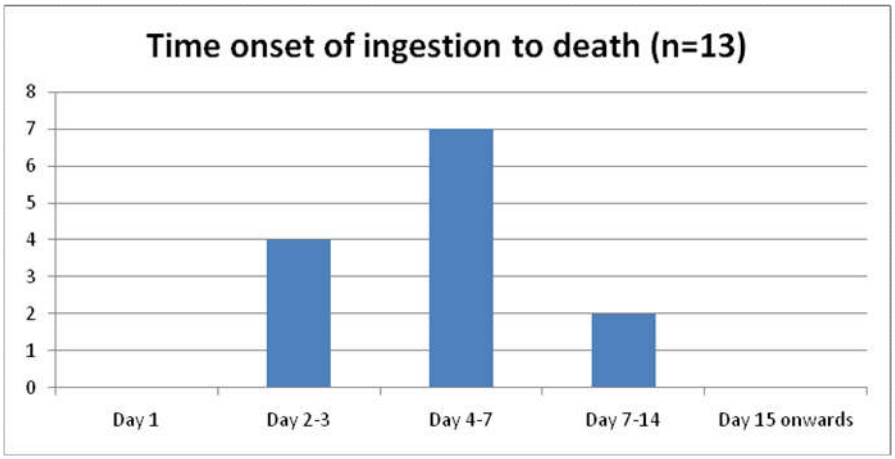


Figure 5. Distribution of time onset of ingestion to death (n=13)

Pathogenesis: Paraquat is poorly absorbed (around 1 to 5 %) via oral route in humans. The volume of distribution is 1-2 L/kg. It is unbound to plasma proteins with a mean distribution half-life of five hours and a mean elimination half-life of 84 hours (Houze, 1990). Paraquat is not actively metabolized in the body, with more than 90% being excreted unchanged in urine. The primary target organ of paraquat poisoning is the lung, but it is also distributed in the heart, liver, and kidney. The brain is now recognised as another target organ: after a single injection paraquat is clearly seen in the brain (Cal EPA 2010). There is active, energy-dependent uptake of paraquat by type 1 and type 2 alveolar epithelium in the lungs, via the polyamine uptake pathway (Honoré, 1994). Paraquat leads to the formation of superoxide anions by redox-cycling-process in the presence of NADPH and cytochrome P450 reductase which is more toxic than hydrogen peroxide (Suntres, 2002). The protective mechanisms such as catalase and glutathione peroxidase are overwhelmed and the resultant oxidative stress cause mitochondrial damage. The hydroxyl radical, formed in the presence of iron, induce lipid peroxidation which causes cell membrane damage and cell death (Jones, 2000). Paraquat thus leads to extensive mitochondria damage of cells through the production of free radicals and oxidative stress, resulting in the interruption of important biochemical processes, cell death, and multi-organ failure.

A wide variety of lethal doses have been reported in literature some in terms of ions and some in terms of concentration.

Oral: Kemi (2006): • Oral LD50 rat = 40-200 mg/kg • Oral LD50 mouse = 120 mg/kg • Oral LD50 guinea pig = 22-80 mg/kg • Oral LD50 rabbit = 49-150 mg/kg • Oral LD50 sheep = 50-75 mg/kg • Oral LD50 cat = 26-50 mg/kg • Oral LD50 dog = 25-50 mg/kg • Oral LD50 monkey = 50 mg/kg • Oral LD50 human = 40-60 mg/kg. According to Wesselings *et al*, the lowest fatal dose recorded for humans is 17 mg/kg, but even lower doses may be fatal for children.

METHODOLOGY

The study is a retrospective study conducted at our Tertiary Care Hospital for a period of 9 months. The history, time onset from ingestion to hospitalization, initial managements at other hospitals prior to referral, presenting symptoms, investigations and death records were reviewed and data analysed anonymously. Quantification of the amount of paraquat ingested could not be established accurately. Patients having serum creatinine≥1.5 mg/dl were classified to have Acute Kidney Injury, those with elevated ALT and serum Bilirubin and/or INR≥1.5 were classified as having liver failure and those with Pa02≤60mmHG were classified to have Acute Lung Injury. Multiple Organ Dysfuction were also noted when multiple organs were involved. The patients were clinically screened for any evidence of infection and routine blood & urine investigations were performed in all patients. It is worth mentioning that in a significant number of patients admitted with suspected paraquat ingestion, documentation of intake of the same could not be verified and were subjected to PM examination. They were not included in the data.

RESULTS

A total of 22 patients were admitted or later confirmed with a diagnosis of paraquat poisoning. 10 were male and 12 were female. Unfortunately only 5 among those admitted survived. 3 among those admitted left against medical advice. All patients had ingested paraquat orally and the intent was suicidal in 18 of the cases and accidental in 4 out of the 22 admitted. The age distribution of those admitted is shown below with the majority in the age group of 20-30 yrs. The time onset from ingestion to hospitalization is depicted in figure below with the majority of presentation being between 1-3 days. The predominant presenting clinical features included vomiting(100%), oral ulcerations, odynophagia, dysphagia, burning epigastric pain, oliguria and AKI (19 out of the 22 patients) with majority needing dialysis, respiratory distress

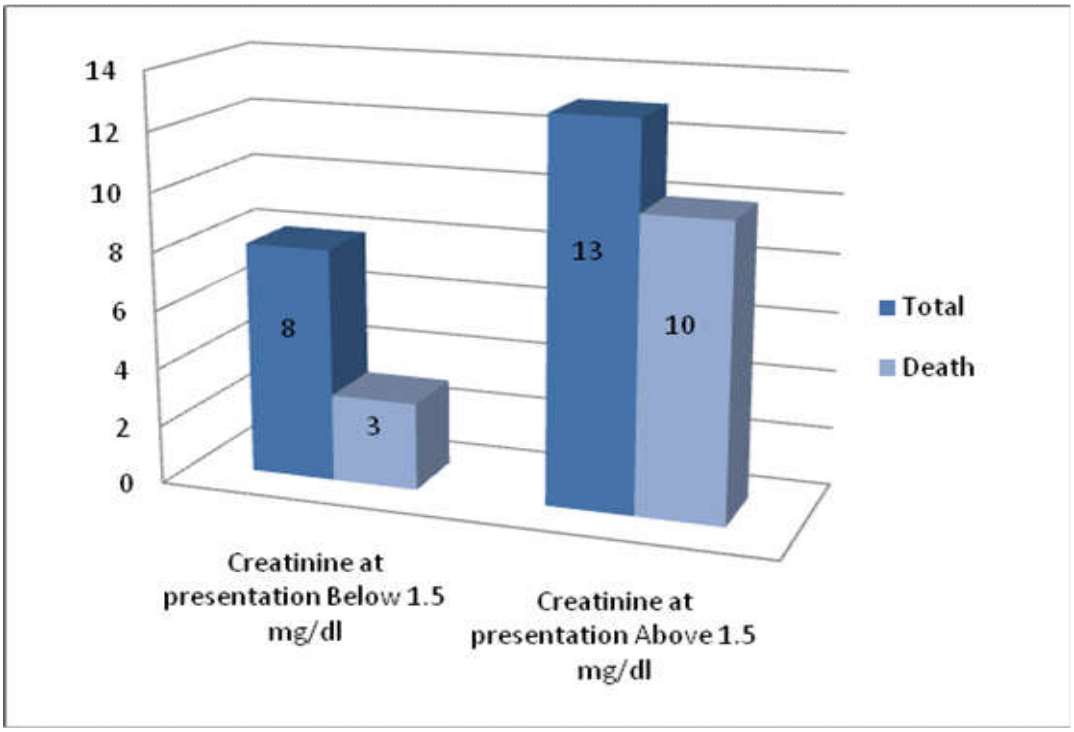


Figure 6. Distribution of mortality based on creatinine values at presentation

needing ventilator support, jaundice, altered sensorium, hypotension etc. Majority had multiorgan dysfunction syndrome and finally succumbed to death (67%). Majority of the death occurred 12 hours after ingestion. Out of the survivors, only 3 were asymptomatic and developed AKI which resolved with conservative management and discharged. Rest 2 had features of ARDS, AKI and mild transaminitis which improved conservatively. Quantification of the amount of paraquat ingested could not be established accurately. The mean duration of admission till death was 4.8 days. The overall picture is depicted below.

Among those hospitalized, 11 patients were shifted to the Intenstive Care Unit and only 3 of them survived. Although the mortality was higher in patients with creatinine at baseline ≥1.5mg/dl, there was no significant statistical difference between the two groups. Also, there was no correlation found between the creatitine values at presentation and the outcome of the patient (spearman co-efficient ρ=0.157 and p-value>0.05)

DISCUSSION

Paraquat poisoning is of toxicological importance in India especially eastern India, as it is widely used as a weedicide.

The fatality rate of paraquat poisoning is very high as there is no specific antidote. According to Raghavendra *et al*, patients who received early haemoperfusion (< 4-6 hours) were more likely to have a better outcome of survival as compared to those who received late haemoperfusion (>4-6 hours)(Rao, 2017). After ingestion, Paraquat is actively sequestered in the lungs and causes free radical damage which leading to lipid damage in the cell membranes, ultimately resulting in pulmonary fibrosis and hepato/nephrotoxicity (Tominack, 2002; Clark, 1966; Hargreave., 1969; Suntres, 2002; Lock, 2001) Gastrointestinal absorption of paraquat is poor with peak plasma concentration of paraquat about 1 to 2 hours after ingestion (Tintinalli *et al*., 2016). As there is no specific clinically proven antidote for paraquat poisoning, supportive treatment is given to avoid free radical injury. Conventional treatment includes nasogastric tube fixation, gastric lavage with normal saline, charcoal-sorbitol lavage, forced alkalinized diuresis and hemodialysis or hemoperfusion. Hemoperfusion with activated charcoal has been found to be effective if initiated within 4 hours of ingestion. Ironically, oxygen supplementation may have a deleterious effect because it increases the number of toxic radicals. Oxygen should, therefore, be given only to correct hypoxemia when pO2≤70mmHg (Arts, 2006). Some antioxidants like vitamins C and E have been clinically used to protect against free-radical toxicity. N-acetyl cysteine is also used as an antioxidant because of its free radial scavenging property, and it will increase intracellular glutathione levels (Dinis-Oliveira, 2008). According to the results of some Randomized Clinical Trails, treatment with glucocorticoid plus cyclophosphamide in addition to standard treatment, have some benefits in patient with paraquat-induced pulmonary fibrosis (Li, 2010) Subsequent management includes antibiotics for supervening infection, supporting renal function with hemodialysis or filtration. Despite being a serious and fatal threat to population at large, there are no recommended guidelines or treatment protocol for paraquat poisoning. It is therefore a necessity to devise strategy regarding production, sale, distribution, health education and treatment protocol against paraquat poisoning.

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