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Multiorgan Failure due to Paraquat Poisoning: Case Report & Review of Literature

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Introduction

Paraquat is a broad spectrum liquid herbicide. Structurally, it is a bipyridyl compound (1, r-dimethyl-4, 4'-bipyridium dichloride). It is sprayed on unwanted weeds and other vegetations before planting crops. It is a fast-acting, nonselective compound, which destroys tissues of green plants on contact and by translocation within the plant. Paraquat exerts its herbicidal activity by inhibiting reduction of NADP to NADPH during photosynthesis. This disruption leads to the formation of superoxide anion, singlet oxygen, and hydroxyl and peroxyl radicals. These reactive oxygen species (ROS) interact with the unsaturated lipids of membranes, resulting in the destruction of plant organelles, inevitably leading to cell death[1]. It is produced commercially as a brownish concentrated liquid of the dichloride salt in 20% strength under the trade name of "Weedout" and for horticultural use as brown granules called "Weedol" at about 5% concentration. Even though, paraquat is extensively used in agriculture, few cases have been reported in India. It's poisoning is associated with very high mortality. We are reporting one case of acute Paraquat poisoning from Safdarjung Hospital, New Delhi.

Case Report

Diagnosis of paraquat poisoning is often made on circumstantial evidence as in this case patient had a bottle containing paraquat.

An apparently healthy 45-year-old female presented with alleged history of accidental ingestion of paraquat. The patient reported to emergency department of Safdarjung hospital, three days after paraquat ingestion. She had consumed about 10 ml of the herbicide following which she had 15 episodes of vomiting and loose stools. The patient also complaint of discomfort in throat and epigastrium and pain abdomen. After consumption of the poison the patient had a single episode of hematemesis. There was no history of loss of consciousness or seizures following ingestion. There was no history of difficulty in breathing or decrease in urine output or bleeding from any site. The patient had no significant medical or surgical history.

At the time of admission, she was conscious oriented and alert. Her BP was 171/91 pulse rate

was 88 per minute. Saturation of oxygen was 87% on O2 support. Examination of oral cavity showed mucosal ulceration of tongue and lips but there was no oral bleeding. Chest examination -bilateral air entry was present, wheeze present. Cardiovascular examination was normal. Abdominal examination and CNS examination was apparently normal.

Skiagram showed prominent bilateral bronchovascular markings. Initially her CBC, electrolytes, liver function test and kidney function test were within the normal limits. During the hospital stay, blood urea and creatine increased to 332 mg% and 8.4 mg% respectively (Table 1).

Liver function also deteriorated subsequently. SGOT and SGPT showed a significant increase. INR also increased progressively. ECG and 2D echo were normal.

The treatment included L-ornithine, L Aspartate injections, n-acetyl cysteine, methylprednisolone and cyclophosphamide. She was also given empirical antibiotics i.e. ceftriaxone , pipracillin-tazobactum and clindamycin injection, nebulization with salbutamol and for hypertension tablet amlodipine was started. Injection pantoprazole was also given.

Patient had presented late, so no activated charcoal and nasogastric suction (decontamination) was done.

Liver function and kidney function progressively deteriorated. The patient developed MODS and AKI, which was supported by haemodialysis. But the patient's condition for the deteriorated and ultimately collapsed and was declared dead after7 days of ingestion.

Table 1 Changes in blood, liver and kidney function of the patient 3,4,5,6 and 7 days following ingestion.

INV/DATE	Day 3	Day 4	Day 5	Day 6	Day 7
Hb	11.8	10.8	11.6	12.6	10.7
TLC	13200	10700	12700	16200	10800
PLT	288000	236000	287000	332000	328000
Na	134	135	138	141	154
K	4.1	4.0	3.9	4.4	3.8
BU	184	209	261	280	332
S.Cr	6.0	6.7	7.6	7.8	7.9
SGOT	303	366	452	471	423
SGPT	328	358	412	389	288
ALP	483	644	1267	1844	1986
INR	1.1	1.2	1.4	1.5	1.71
S.bil	5.2	6.0	10.1	14.4	16.3

Fig 1- Shows the toxin- paraquat consumed by the patient.

Fig 2

Discussion

Paraquat (1,1' – dimethyl-4, 4'-bipyridinium) was introduced in 1962. It is a widely used contact herbicide with a good safety record when used properly 1. It came into disrepute because of accidental or intentional ingestion or large exposure to skin or mucous membrane can cause toxicity leading to high mortality. It is inactivated by adsorption to clay in the soil. The toxicity of paraquat is through redox cycling, leading to generation of superoxide anions. These may react to form hydrogen peroxide and subsequently the highly reactive hydroxyl radical, which is thought to be responsible for lipid peroxidation and cell death. A second contributing factor to toxicity is the depletion of nicotinamide adeninedinucleotide phosphate with bound hydrogen ion(NADPH), as both paraquat redox cycling as well as hydrogen peroxide detoxification via glutathione isNADPH dependent.[(1)]

Paraquat is a highly toxic compound and the fatality rate of paraquat is between 60% and 80%[(2)] because of lack of a specific antidote. A paraquat dose of 30 mg/kg may be fatal, which is equivalent to 8–10 mL of the 20% solution sold commercially[(3)]. Our patient consumed around 10 ml of paraquat, which proved to be fatal. Paraquat has been shown to cause significant damage to organs, including the lung, liver, myocardium and kidneys, with the highest concentration of paraquat found in the lungs[(4)]. The prognosis of patients with multiple organ failure caused by fulminant poisoning (>40 mg/paraquat ion per kg of body weight) is extremely dangerous and affected individuals may succumb within hours to a few days following ingestion[(5,6)]

Although it has been found to be safe for occupational use, paraquat poisoning usually occurring through ingestion of the poison either accidentally or intentionally in an attempt to suicide. Paraquat is banned or rarely used in the developed world; however, in developing countries paraquat continues to be used and paraquat poisoning remains a major cause of mortality among patients with acute poisoning.[(4)]

The prognosis of patients with multiple organ failure caused by fulminant poisoning (>40 mg/paraquat ion per kg of body weight) is extremely dangerous and affected individuals may succumb within hours to a few days following ingestion[(5,6)].

The clinical course of paraquat poisoning depends upon the amount ingested. Initial phase of moderate to severe poisoning is characterized by reversible liver and renal failure. The most frequent routes of exposure to paraquat, either accidentally or intentionally, in humans and animals are following ingestion or through direct skin contact. If ingested, paraquat induces a burning sensation of the mouth and throat, followed by gastrointestinal irritation, subsequently resulting in abdominal pain, loss of appetite, nausea, vomiting, and diarrhoea. Direct contact with paraquat solutions or aerosol mists may cause skin burns and dermatitis. Paraquat splashed in the eyes can irritate, burn, and cause corneal damage and scarring of the eyes. Due to its low vapour pressure and the formation of large droplets, inhalation of paraquat spray used in the open environment has not been shown to cause any significant systemic toxicity; however, inhalational exposure to paraquat in confined spaces, such as a greenhouse, is known to be associated with fatal pulmonary disease. Irrespective of its route of administration in mammalian systems, paraquat is rapidly distributed in most tissues, with the highest concentration found in the lungs and kidneys. The compound accumulates slowly in the lungs via an energy dependent process. Excretion of paraquat, in its unchanged form, is biphasic, owing to lung accumulation and occurs largely in the urine and, to a limited extent, in the bile .Poisoning with paraquat leads to both local and systemic effects. In an Indian series of 17 patients, the most common symptoms were vomiting (100%), followed by altered sensorium (59%), oral ulceration or dysphagia (53%), dyspnea (41%), or loose stools (24%)[8]. Systemic effects of paraquat are renal and hepatic failure, pulmonary edema

and fibrosis, cardiac failure, shock, convulsions, and multiorgan failure. Involvement of lung in the form of diffuse alveolitis and subsequent pulmonary fibrosis is the hallmark of paraquat poisoning. Acute respiratory distress syndrome because of paraquat usually appears 24–48 h after ingestion[7]. Cause of renal failure is multifactorial-hypovolemia, circulatory failure, septicaemia, and direct toxicity related to redox cycling[4].

Multiorgan failure is often the cause of death in many cases. Experimental animal studies have also suggested the same.

Renal failure may be manifested by proteinuria and oliguria which then progresses to acute tubular necrosis. Haemodialysis or continuous renal replacement therapy have been used for acute kidney injury.

Biphasic injury, initially hepatocellular and later cholangiocellular injury involving small and medium sized bile ducts in portal areas have been seen in experimental and autopsy cases. Liver and kidney injure are potentially reversible.

Paraquat is known to get concentrated in lungs (Pulmonary concentrations can be 10 times higher than plasma). Alveolitis and bronchiolitis have been described in post mortem studies. Severe hypoxemia is known to occur. Lung injury may be exacerbated by giving oxygen, which is generally withheld until Po2 is less than 70mmHg. Delayed injury in form of pulmonary fibrosis has been noticed wither in patients who survived or had delayed death from poisoning.

Thus the injury in paraquat poisoning involves two phases, one is destructive phase of inflammation and oedema and other is proliferative phase in which there is proliferation of fibroblast leading to interstitial fibrosis.

Although various theories have been postulated to explain destructive action of paraquat in the lung, there is no satisfactory explanation for the development of pulmonary fibrosis. Steroid and cyclophosphamide are recommended to prevent pulmonary changes in particular.

Liver enzymes and bilirubin are most commonly only moderately raised. Dilatation of bile canaliculi with decrease of microvilli and thickening of the pericanalicular ectoplasm in the hepatocytes has been seen in electron microscopic study of liver biopsy in paraquat poisoning. Thus bile secretory apparatus in the hepatocytes has been seen in electron microscopic study of liver biopsy in paraquat poisoning. Thus bile secretary apparatus in the hepatocytes as well as biliary epithelial cells could be a target of paraquat or its metabolites.

Kidney is the main target organ responsible for paraquat excretion, which occurs mainly in biphasic manner. This resultant kidney injury may reduce this elimination of paraquat and increase its toxicity in other organs.

Early rapid phase and late phase, slow elimination phase which may be possibly due to renal tubular damage caused by paraquat itself.

Treatment

At present there is no antidote to paraquat poisoning. Isolated case reports of survivors have been related to early presentation, active decontamination and small mass of the dose.

Gastrointestinal decontamination is recommended in all patients who present early, especially within 1 hour of ingestion. Early and aggressive decontamination using activated charcoal 50-100gm or 0.5-1g/kg in children have proved to be useful. Hemoperfusion is said to decrease paraquat levels if initiated within 4 hours of ingestion but there is insufficient data to support any survival benefits in humans. General supported measures like Fullers earth is recommended.

IV fluids, care of mouth, maintenance of blood pressure, analgesics are given. Pulse therapy of cyclophosphamide 500mg for 2 days is given. Dose is modified if renal failure occurs.

There are no definite animal studies that have shown benefits of immunosuppression, however some authors have shown benefits of such treatment in small randomised trials.

Several antioxidants have been studied as potential antidotes for paraquat poisoning. Since there have been small number of studies, optimal dose of these have not been defined. Both experimental and invitro studies have demonstrated benefits of using acetylcysteine in paraquat poisoning. Some have used 2gm immediately and then 1gm TID or 600mg TID has also been used. However, there is insufficient information to indicate effectiveness of any dose, if any.

Some groups have advocated vitamin C 4000mg/day and Vitamin E 250micro gm / day as antioxidants, even though efficacy is unproven.

Based on experimental animal studies and sparse human data, early decontamination, immunosuppression therapy and use of acetylcysteine and vitamin C or vitamin E have promising mechanism to consider in the treatment protocol. In the absence of definite role of such treatment, it seems early and aggressive decontamination, to prevent further absorption of paraquat may not be the most accepted treatment. Further studies need to be done to find out any antidote and or effective treatment, both of which are lacking today. Such case reports are likely to incite greater interest in finding out lifesaving treatment protocol in randomised studies

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