Two Cases of Paraquat Poisoning from Himachal Pradesh

S Raina*, V Kumar*, S S Kaushal**, D Gupta***

Abstract
Paraquat (1, 1'-dimethyl-4, 4'-dipyridylium) is a broad spectrum, contact, liquid herbicide associated with both accidental and intentional ingestion, leading to severe and often fatal toxicity. Despite its free availability in the Indian market for use by agriculturists, it is an uncommon poisoning in India with only a few case reports described from India. We report two cases of fatal paraquat poisoning from a tertiary care hospital in the northern state of Himachal Pradesh, India.

Key words: Paraquat, Poisoning, Herbicide.

Introduction
Paraquat is a quaternary nitrogen herbicide that is sprayed on unwanted weeds and other vegetations before planting crops. It is a fast-acting, non-selective 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, as well as 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. The strong affinity for adsorption to soil particles and organic matter is one of the major advantages in introducing paraquat as a herbicide because it limits its bioavailability to plants and microorganisms. Moreover, paraquat is not mobile in most soils and the portion that does not become associated with soil particles can be decomposed to a non-toxic product by soil bacteria; thus, paraquat does not present a high risk of groundwater contamination. However, paraquat has been demonstrated to be a highly toxic compound for humans and animals and many cases of acute poisoning and death have been reported over the past few decades. It is produced commercially as a brownish concentrated liquid of the dichloride salt in 10 - 30% strength under the trade name of ‘Gramoxone’ and for horticultural use as brown granules called ‘Weedol’ at about 5% concentration. Paraquat poisoning has been widely reported worldwide, but only a few case reports are described in literature from India. We report two cases of fatal paraquat poisoning from the northern Indian state of Himachal Pradesh, who were admitted in a tertiary care hospital. Both the patients were agriculturists and belonged to a vegetable growing area of the state where ‘Gramoxone’ is freely available for use in the fields. On extensive literature search no case of paraquat poisoning was found to be reported from this state of India.

Case report

Case No. 1
A forty-year-old male patient was admitted in the medical ward with history of ingestion of 5 ml of paraquat dichloride (Gramoxone - 24% SL) six days back. The patient had vomited immediately after ingestion of paraquat. There was no history of oliguria. Clinical examination revealed oral erosions and icterus. Rest of the examination was normal. Investigations showed serum urea as 292 mg/dl and creatinine as 9.8 mg/dl on admission. Total serum bilirubin was 36.9 mg% and conjugated was 24.0 mg%. The transaminases were raised (SGOT - 300 IU and SGPT - 311 IU). The alkaline phosphatase was 426 K AU. The patient was managed conservatively for five days along with two sessions of haemodialysis. Thereafter, the patient developed features of adult respiratory distress syndrome and died on ventilatory support. On autopsy, lungs showed bilateral emphysematous bullae with extensive haemorrhagic areas. The brain, heart, liver, and kidneys were congested. Histopathological examination was not done.

Case No. 2
A twenty-one-year-old female patient was admitted in the medical ward with history of ingestion of 20 ml of

*Senior Resident, **Professor and Head, ***Associate Professor, Department of Medicine, Indira Gandhi Medical College, Shimla - 171 001, Himachal Pradesh.
paraquat dichloride (Gramoxone - 24% SL) three days back. History of oliguria was present for last two days. On examination, she had tachycardia and was tachypnoeic. Oral erosions and icterus were present. On nervous system examination, deep tendon reflexes were absent. Rest of the examination was normal. The serum urea was 253 mg/dl and creatinine was 11.0 mg/dl. Total serum bilirubin was 6.2 mg% and conjugated was 4.2 mg%. The transaminases were raised (SGOT - 199 IU and SGPT - 210 IU). The alkaline phosphatase was 207 KAU. The serum uric acid was 253 IU. The alkaline phosphatase was 207 KAU. The patient was managed conservatively for two days including one session of haemodialysis, and became haemodynamically unstable with features of adult respiratory distress syndrome and died despite ventilatory support. On autopsy, stomach showed erosions and patchy haemorrhages. Histopathological examination was not done.

**Discussion**

Acute paraquat self-poisoning is a significant problem in parts of Asia, the Pacific and the Caribbean. The most frequent routes of exposure to paraquat, either accidentally or intentionally, in humans and animals are 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. Biotransformation of paraquat is, in general, poor in all species studied and the excreted compound is unchanged. The primary injury caused by paraquat to mammalian systems occurs in the lung, where paraquat is accumulated through a process of active transport in the Clara cells and alveolar type I and II epithelial cells. The paraquat-induced lung injury is morphologically characterised by an early destructive phase, in which the alveolar type I and type II epithelial cells are damaged; and a second proliferative phase defined by alveolitis, pulmonary oedema, and infiltration of inflammatory cells. In addition to the lung, paraquat administration has been shown to injure other major organ systems, but to a lesser extent. Pathological changes have been observed in the liver, kidney, and heart at high doses; but death is usually associated with respiratory insufficiency injury. The mechanisms of paraquat toxicity involve: the generation of the superoxide anion, which can lead to the formation of more toxic reactive oxygen species, such as hydrogen peroxide and hydroxyl radical; and the oxidation of the cellular NADPH, the major source of reducing equivalents for the intracellular reduction of paraquat, which results in the disruption of important NADPH-requiring biochemical processes. Treatment involves removal of ingested paraquat by immediately induced emesis or by gastric lavage in a health care facility. Clay (Fuller’s earth) and activated charcoal are effective adsorbents. Administer repeated doses of 60 gm of activated charcoal by gastric tube every two hours for three or four doses. Supplemental oxygen should be withheld unless the pO$_2$ is less than 70 mmHg because oxygen may contribute to the pulmonary damage which is mediated through lipid peroxidation. Since the principal biochemical mechanism for lung damage is initiated by oxygen free radicals produced by peroxidation, clinicians have tried a number of anti-oxidant treatments in the hope that they might interfere with the process. Unfortunately, none of the studied treatments, including controlled hypoxia, superoxide dismutase, vitamins C and E, N-acetylcysteine, desferrioxamine, and nitrous oxide, has been proven to be effective. However, recent evidence regarding the use of immunosuppressive therapy with glucocorticoids and cyclophosphamide in the management of lung injury in patients with severe paraquat poisoning has been encouraging. Two randomised controlled trials have suggested a definite trend in benefit with immunosuppressive therapy in patients with moderate to severe poisoning. In an Indian study, five patients with...
severe and fulminant paraquat poisoning were started on the day of hospital admission on intravenous methylprednisolone 15 mg/kg/day for three consecutive days, intravenous cyclophosphamide 10 mg/kg/day for two consecutive days, followed by intravenous dexamethasone four milligrams thrice a day until recovery or death. Two out of the five patients did survive. In another meta-analytical review evidence of benefit was shown with the use of immunosuppression in all forms of studies, and hence supported the use of immunosuppression in patients with severe paraquat poisoning. A systematic review performed in 2003 did not find good evidence of benefit or harm from immunosuppression, so a large randomised controlled trial is required to affirm the role of immunosuppression in paraquat poisoning. Diquat is another dipyridyl herbicide widely used in agriculture and has early corrosive effect similar to paraquat. Diquat is not selectively concentrated in lung tissue so pulmonary injury is less prominent and no progressive pulmonary fibrosis has been noted. However, toxic effects on central nervous system and kidneys are prominent. Prognosis in paraquat poisoning is largely dependent on the amount of paraquat absorbed. Rapid identification of the symptoms of paraquat toxicity (burns or ulceration at the site of ingestion or injection, acute respiratory distress, and renal failure) can facilitate early treatment intervention to limit absorption. According to our knowledge these are first cases of paraquat poisoning reported from the state of Himachal Pradesh, India. These cases are reported to highlight the high mortality rate associated with Paraquat poisoning in spite of advances in treatment and supportive care.

References