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Successful Management of Paraquat-Induced Multiorgan Dysfunction Syndrome with Intravenous N-Acetyl Cysteine.

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ABSTRACT

Paraquat, a commonly used herbicide, has been associated with high mortality rates when consumed either accidentally or intentionally. The proposed mechanism is free radical-mediated cell damage, leading to multisystem failure, especially involving the lungs and the kidneys. Ideally, diagnosis should be made early and treatment should be initiated as soon as possible. Prognosis of the patient depends on the quantity of the herbicide consumed. Moderate to severe paraquat poisoning is associated with dire consequences. Given below is a case of paraquat poisoning thatled to the development ofmultiorgan dysfunction syndrome that was successfully managed with hemoperfusion and parenteral N acetyl cysteine as given for paracetamol poisoning.

Keywords: Herbicide, free radical, haemoperfusion, N-acetylcysteine, antioxidant

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INTRODUCTION

Paraquat is a freely available, commonly used herbicide. It acts during photosynthesis by inhibiting conversion of NAPD to NADPH. This disruption leads to generation of reactive oxygen species, damaging plant organelles, thus imparting herbicidal effect. On contact with soil, paraquat is decomposed to a harmless metabolite by bacteria, thereby preventing contamination of ground water [1].

In Asia, Caribbean and Pacific, paraquat self-poisoning is a significant issue. Poisoning occurs either due to ingestion or due to contact. Ingestion of this herbicide may cause nausea, vomiting, diarrhea and abdominal distension whereas; contact may lead to dermatitis and burns. There have been instances of corneal damage when paraquat was accidently splashed to the eye. Inhalation of paraquat vapors has been known to cause fatal pulmonary disease especially in closed spaces like greenhouses. Paraquat poisoning may lead to hepatic, cardiac or renal failure, pulmonary fibrosis, shock, haemolyticuraemic syndrome, etc [2].

There are three degrees of paraquat poisoning [3]:

a) Mild, when the ingested quantity is less than 20mg of paraquat ion/kg, usually asymptomatic, or patient has mild gastrointestinal (GI) symptoms,

b) Moderate to severe, when the ingested quantity is 20-40mg of paraquat ion/kg, where the patient has GI symptoms, preceding kidney failure and lung fibrosis,

c) Acute fulminant poisoning, when the ingested quantity is more than 40mg of paraquation/kg, where the patient develops multiorgan dysfunction, which can be fatal.

Paraquat poisoning is associated with very high mortality rates due to its inherent toxicity and also, due to the lack of effective management modalities. The existing treatment plan includes a combination of haemoperfusion, anti-oxidants and immunomodulation. In spite of all these tools, mortality rates are very high [4].

CASE REPORT

An18-year-old girl, with no premorbid conditions, was admitted with history of alleged consumption of 60 mL of paraquat poison. Before coming to our hospital, she was taken to a peripheral hospital, where a gastric lavage was given. She presented about 12 hours after ingestion of the herbicide. On arrival, she was conscious, oriented. Vital signs showed tachycardia but normal blood pressure. Systemic examination was within normal limits. On close physical examination, hesitation cutswere seen onher forearm. On the second day after her admission,she complained of severe retrosternal chest pain that occurred due to esophageal erosions. Since free radical mediated damage is the pathogenesis involved, N-acetylcysteine therapy was initiated. As there is no literature on the dosage of N-acetylcysteine for paraquat poisoning, it was administered as per the standard protocol for treatment of paracetomol poisoning (Initial loading dose of 150mg/kg over 60 minutes, 50 mg/kg over the next four hours and 100mg/kg over the next 16 hours). Laboratory tests showed thather total leucocyte countwas elevated (23,800 cells/cu.mm.), for which she was started on intravenous ceftriaxone 2gper day. Her serum creatinine level on admission was 1.6mg/dL. A nephrologist's opinion was sought, and the patient was started on the first cycle of haemoperfusion. On the 3rd day following admission, the patient had an episode of hematemesis and was started on pantoprazole infusions. Oral Benzocaine was applied for oral mucosal erosisons and antacids syrup with oxetacaine administered for gastric erosisons and pain.Her platelet count had dropped to 77,000 cells/cu.mm., and she had moderate hypokalemia, for which she was kept managed with intravenous potassium replacement..Pantoprazole infusion was started and IV potassium correction was given during the second cycle of haemoperfusion.The following day (Day 3 after consumption)her platelet count dropped further to 15,000 cells/cu.mm for which four units of platelets were transfused. With these measures, on the subsequent days(day 4), platelets, potassium and total leucocyte counts had normalized, but her hemoglobin level had significantly dropped to 8.5g/dL, for which 1 unit of packed RBCs was transfused. However, (on day 5) she had 2 episodes of spontaneous hypoglycemia that was managed by administering parenteral dextrose and maintainence intravenous glucose.Platelet countsdropped again (11,000 cells/cu.mm.) and fourunits platelets wereadministered.Lactate dehydrogenase (LDH) level was 912U/L (normal range being 140-280 U/L). Her liver

function tests were normal throughout. During her stay in the ICU, she underwent 5 cycles of haemoperfusion. Miraculously, despite development of acute kidney injury, hypoglycemia, severe anemia and thrombocytopenia requiring transfusion, the patient recovered.At the time of discharge, the patient recovered, with a serum creatinine of 0.9 mg/dL, serum potassium of 3.6 mEq/L, and a platelet count of 3,19,000 cells/cu.mm. Her chest x ray showed no features of ARDS and she did not require any supplemental oxygen during the course of her illness.

DISCUSSION

Management of paraquat poisoning includes gastrointestinal decontamination with gastric lavage, enhancing elimination using haemoperfusion orhaemodialysis, which should be initiated as early as possible, and antioxidants like N-acetylcysteine (NAC), vitamin C, vitamin E, etc [4].

The major mechanism of toxicity in paraquat poisoning is the generation of oxygen free radicals. Paraquat is metabolized by numerous enzyme systems like nitric oxide synthase, xanthine oxidase, cytochrome p-450, NADH-ubiquinone oxido-reductase to produce paraquat mono-cation radical. Intracellularly, this radical is re-oxidized and super oxides are generated. Further, due to Fenton reaction, hydroxyl radicals are also produced. Further, peroxynitrite, a very strong oxidant is produced. Production of these highly reactive nitrite and oxygen species causes multi-organ toxicities.[4]Keeping this in mind, this patient was initiated on NAC therapy.NAC reduces serum malondialdehyde levels, thereby reducing superoxide production and increasing glutathione concentrations [5]. Studies have shown that liposomal NAC (L-NAC) is better than conventional NAC, as L-NAC has increased intracellular concentration due to liposomal delivery [6].

Other treatment modalities like immunosuppression in paraquat poisoning using corticosteroids, cyclophosphamidehave been tried, but their role has not been definitely established [7].

CONCLUSION

Paraquat poisoning is a physician's nightmare as it is associated with a high mortality rate. The secret for successful management lies with an early diagnosis followed by immediate intervention with gastric lavage, haemoperfusion and initiation of antioxidant therapy so as to prevent the development of multi-organ failure. Once the multi-organ dysfunction sets in, management becomes tricky and the physician usually ends up fighting a losing battle.

The case highlights the importance of early and aggressive management in patients with paraquat poisoning. Larger studies need to be undertaken to ascertain the role of high dose intravenous N acetyl cysteine in the management of paraquat poisoning. This young girl survived only due to the timely hemoperfusion, intravenous N acetyl cysteine and transfusion of blood products preventing catastrophic hemorrhage. From a public health perspective, counselling and educating the farmers and people at risk of consuming paraquat is of paramount importance considering its potentially devastating effects.

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