# Acute Kidney Injury Following Paraquat Poisoning in India

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**Keywords.** paraquat, acute kidney injury, multiorgan failure

Paraquat is highly toxic to human and is widely used in agriculture as a contact herbicide. Paraquat poisoning is associated with high mortality varying from 35% to 50%. Six cases of paraquat poisoning were treated in our center. Acute kidney injury developed in all the cases and mortality was 66%. Respiratory and multiorgan failure are the main causes for mortality.

IJKD 2013;7:64-6
www.ijkd.org



Paraquat (1,1′-dimethyl-4,4′-bipyridylium dichloride) is widely used as a herbicide. Toxicity is usually seen following ingestion, and may range from mild (ingestion of less than 20 mg of paraquat ion per kilogram of body weight) to fulminant (> 40 mg),[1] with the latter commonly proving fatal. In addition to intense local irritation of the mouth, oropharynx, and oesophagus, multiple organ (cardiac, respiratory, hepatic, and renal) failure may occur, although pulmonary features predominate and are the usual cause of death. We report our experience of acute paraquat poisoning with acute kidney injury.

All patients with paraquat poisoning admitted to the intensive care units in Hassan (Karnataka State, India) between 2011 and 2012 were studied. The diagnosis was based on the history, verification of the ingested herbicide and urine examination for the presence of paraquat. To examine the urine sample, 10 mL of patient's urine was mixed with 2 mL of a 1% solution of sodium dithionite in 1 N sodium hydroxide; a blue color indicates the presence of paraquat. Acute kidney injury was defined by a serum creatinine level greater than 1.5 mg/dL.

Six patients who had exposure to paraquat were included in this study. Their characteristics are summarized in the Table. Most of the patients were young men around the age 30 years. Five of the patients had paraquat solution ingested for suicidal attempt. The degree of poisoning was assessed by the quantity of paraquat concentrate ingested, ie, less than 20 mL as mild, 20 mL to 100 mL as moderate, and greater than 100 mL as severe. Three patients had severe exposure to paraquat (100 mL to 500 mL). Pulse methylprednisolone of 1 g/d for 3 consecutive days followed by oral dexamethasone, 8 mg thrice a day, was given in an attempt to suppress the inflammation, and to prevent absorption of paraquat from the gastrointestinal tract, 60 mg in 200 mL of 20% mannitol, was given in a selected patient who was referred very early to our hospital.

All the 6 patients developed acute kidney injury. The mean serum creatinine level was 5.3 mg/dL. Five of 6 patients required hemodialysis. Recovery of kidney function occurred in 2 patients; 1 patient had complete recovery, while the other patient had partial recovery of his kidney function. The other organ systems involvement included respiratory (100%), hepatic (50%), gastrointestinal tract (33.3%), and multiorgan (66.7%) involvement. Four patients died during hospitalization. Respiratory failure and multiorgan failure were the main causes for mortality.

Paraquat is highly toxic to human. The chemical structure of paraquat is 1,1′-dimethyl-4,4′-bipyridinium. It belongs to the group of dipyridyl herbicides. In plants, it disrupts photosynthesis by inhibiting the electron transport chain. It has low environmental toxicity due to rapid deactivation upon soil contact.[2] Exposure to paraquat can be due to intentional ingestion or occupational exposure, eg, dermal and eye contact. A dose of 3 g to 6 g is considered to be fatal for adults.[2] Paraquat is a water soluble quaternary ammonium derivative. It is poorly absorbed by the oral route in humans. Around 1% to 5% of an oral dose is absorbed in the intestines. The volume of distribution is 1 L/kg to

Characteristics and Clinical Data of Patients

| Patient | Age, y | Gender | Exposure | Amount of Paraquat | Time to Admission | Organ Involvement | Therapeutic Modalities | Outcome |
|---|---|---|---|---|---|---|---|---|
| 1 | 35 | Male | Suicide | 100 mL | 2 days | Renal, respiratory, hepatic, gastrointestinal | Methylprednisolone, hemodialysis, assisted respiration | Death of respiratory failure 4 days after ingestion of paraquat |
| 2 | 37 | Male | Suicide | Mouthful | 5 days | Renal, respiratory, hepatic, gastrointestinal | Methylprednisolone, hemodialysis, assisted respiration | Death of respiratory & multi organ failure 6 days after ingestion of paraquat |
| 3 | 28 | Male | Suicide | 50 mL | 3 days | Renal, respiratory | Activated charcoal, methylprednisolone, hemodialysis, assisted respiration | Death of respiratory & multi organ failure 4 days after ingestion of paraquat |
| 4 | 28 | Male | Accidental ingestion | A few drops | 5 hours | Renal, respiratory | Gastric lavage, activated charcoal, intravenous furosemide, hypoxic breathing mixture, mannitol, normal saline, methylprednisolone | Survival, kidney function gradually improved to normal |
| 5 | 35 | Female | Suicide | A large cup | 3 days | Renal, respiratory | Methylprednisolone, hemodialysis, assisted respiration | Death of respiratory and multiorgan failure 7 days after ingestion of paraquat |
| 6 | 33 | Male | Suicide | A half-spoonful | 1 day | Renal, respiratory, hepatic | Gastric lavage, activated charcoal, intravenous furosemide, methylprednisolone, hemodialysis, assisted respiration | Survival, kidney function gradually improved but stabilised at serum creatinine of 2 mg/dL |

2 L/kg.[3] It is unbound to plasma proteins. Plasma paraquat concentration exhibits a mean distribution half-life of 5 hours and a mean elimination half-life of 84 hours.[3] 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.[4]

After ingestion, the greatest paraquat concentration is found in the lungs and the concentration peaks in 5 to 7 hours.[5] Paraquat poisoning causes multiple organ damage. Paraquat selectively accumulates in the lung where free radicals are formed and lipid peroxidation is induced. The capillary endothelial and epithelial cells of the lungs are the main targets of damage. These results in the development of diffuse alveolitis followed by extensive pulmonary fibrosis.[6] The development of pulmonary fibrosis is usually delayed up to 3 to 14 days, but it is progressive.

Paraquat is eliminated mainly by the kidney and acute kidney failure is a recognized complication of paraquat poisoning, with reports of both oliguric[7,8] and nonoliguric[9,10] cases. Beebeejaun and coworkers found proximal renal tubular necrosis by histopathological examination of a fatal case of paraquat poisoning,[11] consistent with the observations of Ecker and colleagues,[12] who observed that functional paraquat renal toxicity was restricted to the proximal nephron in mice. Paraquat poisoning may lead to a Fanconi syndrome with a variety of proximal tubular abnormalities, including glycosuria, phosphaturia and aminoaciduria, as shown in the series of 3 cases reported by Vaziri and colleagues.[13] In our study, all 6 patients had developed acute kidney injury. Four of these patients were given hemodialysis for acute kidney injury. The precipitation of acute kidney injury was mostly multifactorial, ie, hypovolemia, septicaemia, and multiorgan failure.

Two of our patients had partial to complete recovery of their kidney function. Early referrals, absence of multiorgan dysfunction and less amount of paraquat consumption seems to be the key factors for recovery of kidney function. There is no proven antidote for paraquat poisoning.[14] Gastric lavage with 1% bentonite solution has been found to prevent gastrointestinal contamination for patients who present within 1 hour of ingestion

of paraquat. Activated charcoal was found to be effective in lowering serum paraquat concentration when given more than 1 hour after the ingestion of paraquat.[15] Emesis is contraindicated due to the corrosive nature of paraquat. Administration of Fuller's Earth and activated charcoal should be repeated every 4 hourly if tolerated. Human studies have shown hemoperfusion significantly eliminates paraquat from the body.[16] Hemoperfusion is effective if initiated within 4 hours of ingestion. However, these techniques probably do not increase the survival rate in the real situation, because the potentially lethal concentration of paraquat may have already been attained in the highly vascular tissue of vital organs and in the pneumocytes when these techniques are initiated.[17]

Paraquat is not removed by dialysis, and hemodialysis is used only as a supportive treatment for patients who develop kidney failure.[18] The evidence for the effectiveness of immunosuppressive therapies in paraquat poisoning is not yet well established.[18] Chen and colleagues successfully treated a case of severe paraquat poisoning using repeated pulse therapy of methylprednisolone.[19] In our study, pulse methylprednisolone was given in an attempt to suppress the inflammation. The survival rate in our study was 66.7%. Late referral to the hospital, the severity of poisoning and respiratory, kidney and multiorgan failure are the main cause of increased mortality in our study.

Paraquat consumption is a common agent of suicidal poisoning in this part of India, resulting in very high morbidity and mortality. There is no specific antidote for paraquat poisoning and the mainstay of treatment is supportive. Acute kidney injury is the common complication of paraquat poisoning and needs to be recognised and treated promptly.

## CONFLICT OF INTEREST

None declared.

## REFERENCES


1. Vale JA, Meredith TJ, Buckley BM. Paraquat poisoning: clinical features and immediate general management. Hum Toxicol. 1987;6:41-7.
2. Erickson T, Brown KM, Wigder H, Gillespie M. A case of paraquat poisoning and subsequent fatality presenting to an emergency department. J Emerg Med. 1997;15:649-52.
3. Houze P, Baud FJ, Mouy R, Bismuth C, Bourdon R, Scherrmann JM. Toxicokinetics of paraquat in humans. Hum Exp Toxicol. 1990;9:5-12.
4. Hampson EC, Effeney DJ, Pond SM. Efficacy of single or repeated hemoperfusion in a canine model of paraquat poisoning. J Pharmacol Exp Ther. 1990;254:732-40.
5. Bismuth C, Garnier R, Baud FJ, Muszynski J, Keyes C. Paraquat poisoning. An overview of the current status. Drug Saf. 1990;5:243-51.
6. Li S, Li H, Zheng Z, Dong H. [Pathologic characteristics of diffuse alveolar damage induced by paraquat in rat lungs]. Hua Xi Yi Ke Da Xue Xue Bao. 1994;25:337-40.
7. Bullivant CM. Accidental poisoning by paraquat: Report of two cases in man. Br Med J. 1966;1:1272-3.
8. Kodagoda N, Jayewardene RP, Attygalle D. Poisoning with paraquat. Forensic Sci. 1973;2:107-11.
9. Sobha H, Pushpakumari P, Nampoory MR, Visweswaran RK, Ravindran M. Paraquat poisoning with acute renal failure--a case report. J Assoc Physicians India. 1989;37:341-2.
10. Oreopoulos DG, Soyannwo MA, Sinniah R, Fenton SS, Bruce JH, McGeown MG. Acute renal failure in case of Paraquat poisoning. Br Med J. 1968;1:749-50.
11. Beebeejaun AR, Beevers G, Rogers WN. Paraquat poisoning-prolonged excretion. Clin Toxicol. 1971;4:397-407.
12. Ecker JL, Hook JB, Gibson JE. Nephrotoxicity of paraquat in mice. Toxicol Appl Pharmacol. 1975;34:178-86.
13. Vaziri ND, Ness RL, Fairshter RD, Smith WR, Rosen SM. Nephrotoxicity of paraquat in man. Arch Intern Med. 1979;139:172-4.
14. Sandhu JS, Dhiman A, Mahajan R, Sandhu P. Outcome of paraquat poisoning – a five year study. Indian J Nephrol. 2003;13:64-8.
15. Idid SZ, Lee CY. Effects of Fuller's Earth and activated charcoal on oral absorption of paraquat in rabbits. Clin Exp Pharmacol Physiol. 1996;23:679-81.
16. Hong SY, Yang JO, Lee EY, Kim SH. Effect of haemoperfusion on plasma paraquat concentration in vitro and in vivo. Toxicol Ind Health. 2003;19:17-23.
17. Bismuth C, Scherrmann JM, Garnier R, Baud FJ, Pontal PG. Elimination of paraquat. Hum Toxicol. 1987;6:63-7.
18. Wong OF, Fung HT, Kam CW. Case series of paraquat poisoning in Tuen Mun Hospital. Hong Kong J Emerg Med. 2006;13:155-60.
19. Chen GH, Lin JL, Huang YK. Combined methylprednisolone and dexamethasone therapy for paraquat poisoning. Crit Care Med. 2002;30:2584-7.



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Received June 2012
Revised October 2012
Accepted November 2012