CASE REPORT

Case Report: Paraquat poisoning [version 1; peer review: awaiting peer review]

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Abstract
Paraquat (1, 1′-dimethyl-4,4′-bipyridinium) is a commonly used herbicide that is highly toxic when ingested. Ingestion of toxic doses of paraquat has serious complications on the lungs, gastrointestinal tract, kidney, liver, and other organs. Due to its inherent toxicity and the lack of a specific antidote, it has a high case fatality rate. Despite being restricted to commercially licensed users in Nepal, it is a common herbicide causing both intentional and accidental poisoning. Although there have been numerous anecdotal cases of paraquat poisoning in Nepal, no reports have been published in the literature.

We report a case of a 30-year old female, who developed gastrointestinal symptoms like vomiting, diarrhoea and odynophagia, renal and liver injury after accidental ingestion of 10ml of 20% paraquat. Symptoms and organ involvement subsided with timely and appropriate supportive management.

Keywords
paraquat; herbicide; toxicology; poisoning; accidental ingestion; Nepal; Patan hospital
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Introduction
Paraquat (1,1'-dimethyl-4,4'-bipyridinium) is a fast acting contact herbicide that is widely used in agriculture and horticulture industries throughout the world\(^{1–4}\). Its herbicidal properties were discovered in 1858 and it became available for commercial use in 1962\(^{5}\). Initially, it was used to kill marijuana weeds in the United States and Mexico, later it became popular worldwide as it is a cheap and an effective herbicide\(^6\). It is currently the world’s second most popular herbicide, with sales in over 100 countries\(^7\).

Paraquat is extremely toxic for humans as well as animals. Ingestion (intentional or accidental) is the most common route of poisoning\(^8\). Additionally, poisoning via other routes such as dermal or mucus contact\(^9,10\), injection\(^11\) and inhalation\(^12\) have also been reported. The estimated lethal dose in an adult person is around 30 mg/kg\(^13\) or 3–6 g of paraquat ion\(^\text{+}\), which is similar to 10 to 20 ml of a 20% solution.

Clinical symptoms due to paraquat poisoning are mostly due to the formation of intracellular reactive oxygen species, which cause cellular damage through lipid peroxidation, nuclear factor kappa B activation, mitochondrial damage, and apoptosis\(^14\). Paraquat is readily taken up into lung tissue against a concentration gradient, promoting pneumonitis and lung fibrosis\(^15\). Additionally, it affects multiple organs including heart, kidneys, liver, adrenal glands, central nervous system, muscles and spleen causing multiple organ failure\(^16\). The case fatality rate is extremely high, ranging from 50% to 90%, but in situations of purposeful self-poisoning using concentrated formulations, the mortality rate reaches 100%\(^14\). Paraquat’s high case fatality rate is owing to its inherent toxicity as well as due to the lack of an effective antidote. There are no universally-acknowledged standards for treating paraquat poisoning. Treatment varies from supportive care alone to various combinations of immune-modulation, antioxidant therapy, hemoperfusion and hemodialysis\(^14\).

Paraquat has been restricted in many parts of the world as a result of its toxicity\(^17\). Despite being restricted to commercially licensed users in Nepal, it is a common herbicide causing both intentional and accidental poisoning. Although there have been numerous, anecdotal cases of paraquat poisoning in Nepal, no reports have been published in the literature. We report a case of accidental paraquat poisoning from Patan Hospital, Nepal.

Case
A previously well, 30-year-old female presented to the emergency department Patan Hospital, Nepal in August 2021, with the complaint of accidental ingestion of 10ml of paraquat (20%) poison five days previously. She had inadvertently consumed it, mistaking it for a soft drink because it was stored in a Sprite bottle. Following the ingestion, she had multiple episodes of vomiting and diarrhoea for two days. Vomitus contained recently ingested food particles. It was not, however, tainted with bilious material or mixed with blood. The stool was watery in consistency and was devoid of mucous or blood. She also had difficulty swallowing and heartburn began on the third day. Swallowing was more painful for solid food than liquid food. She had also noticed a reduction in urine flow during the previous five days. However, there was no history of fever, seizure, cough, chest pain, shortness of breath, yellowish discoloration of eyes or abdominal distension.

She was conscious at the time of the examination (Glasgow Coma Scale of 15/15). On physical examination, blood pressure (BP) was 140/90 mmHg, however there was postural drop in BP to 110/70mmHg on standing. Her heart rate was regular at 100 beats per minute, respiratory rate was 20 breaths per minute, temperature was 97 degrees Fahrenheit, and oxygen saturation was 98 percent in room air. Examination of the oral cavity showed superficial erosion of dorsum of the tongue with erythematous base which is considered to be a typical presentation of paraquat injury to the tongue (Figure 1). The rest of the systemic examinations were normal.

Basic blood parameters revealed raised urea (153 mg/dL; reference range: 5–20), creatinine (8.6 mg/dL; reference range: 0.6–1.2) and low sodium (128 mEq/L; reference range: 136–146), and potassium (3.3 mEq/L; reference range: 3.5–5.0). Likewise, liver function test showed elevated total bilirubin (2.4 mg/dL; reference range: 0.1–1.0), direct bilirubin (1.2 mg/dL; reference range: 0.0–0.3), aspartate transaminase (AST) (79 U/L; reference range: 10–40), alanine transaminase (ALT) (67 U/L; reference range: 10–40) but normal alkaline phosphatase (ALP) (72 U/L; reference range: 5–20), and normal creatinine (8.6 mg/dL; reference range: 0.8–1.6). Compensated metabolic acidosis with a raised anion gap of 19 was discovered in the arterial blood gas analysis. Urine examination revealed specific gravity of 1.015 (reference range: 1.005-1.030) and urine osmolarity of 261.8 mOsm/kg (reference range 300-900 mOsm/kg), suggestive of intrinsic renal injury. Initial radiography of the chest and electrocardiography were unremarkable. Ultrasound of abdomen showed mild increase in echogenicity in bilateral kidney.

She was admitted in the medical ward with the diagnosis of paraquat poisoning complicated by acute kidney and liver injury. She was managed conservatively with IV fluids for renal injury. In addition, she was treated symptomatically for heartburn with syrup sucralfate and pantoprazole, a proton pump inhibitor and quadragel ointment (a mixture of lidocaine, chlorhexidine, and metronidazole) for her oral lesion.

Figure 1. Patient’s tongue on fifth day of ingestion (at the time of admission).
Throughout her hospital stay, her renal function and liver function gradually improved, and she experienced a general improvement in overall symptoms such as heartburn and difficulty swallowing. Metabolic acidosis resolved as well. No additional symptoms or complications were observed. Subsequently, she was discharged on the fifth day of hospitalization on her request. Her urea and creatinine levels were 62 mg/dl and 3.3 mg/dl respectively, at the time of discharge.

On follow up after ten days of discharge, she reported that her previous symptoms had resolved completely (Figure 2). Compared to the day of admission, her blood values were within normal range (Table 1).

Discussion
Paraquat is a commonly available, cheap herbicide used extensively by farmers in this part of the world. Easy availability and accessibility of paraquat in Nepal could be the reason for its accidental or intentional ingestion. Our patient is a farmer who had stored paraquat in a soft drink container. She accidentally ingested 10 ml of 20% w/v solution, which is considered to be the lethal dose13.

Paraquat readily disseminates in most tissues regardless of the mode of administration. However, the primary organs affected are lung and kidney14,16. Because paraquat is structurally identical to naturally occurring polyamines that are taken up by alveolar cells, it concentrates in type I and II alveolar cells. Fortunately, there was no evidence of pulmonary involvement in our patient because she spat some out immediately due to its offensive smell. Paraquat is also actively released by the kidney, resulting in larger quantities in the proximal tubular epithelial cells16. It causes renal tubular necrosis by inducing vacuolation in the cells of the proximal convoluted tubules16. Our patient has features suggestive of renal injury, as evidenced by decrease in urine output and increase in the level of serum creatinine to 8.6 mg/dl at the time of presentation, which improved during the course of his hospital stay. Paraquat intoxication also results in acute liver injury characterized by persistent elevation of liver aminotransferases and histopathological changes14. Our patient had LFT derangement suggestive of toxic hepatitis, which eventually resolved with conservative management.

The history of ingestion of paraquat, as well as strong supporting evidence from the physical examination, such as the presence of oropharyngeal burns and the subsequent development of acute kidney injury, metabolic acidosis and toxic hepatitis, were used to diagnose paraquat poisoning in our patient. Urine or blood tests might be used to confirm the diagnosis. A plasma concentration of >1.6 pg/ml twelve hours after intake has been determined to be uniformly lethal17. The presence of paraquat in urine has been utilized not only to confirm the diagnosis18, but also to determine prognosis19. However, these tests were not performed on our patient as they are not readily available in our center.

To date, there is no specific antidote for paraquat poisoning. Two crucial factors to consider in the treatment are the amount of paraquat ingested and the time since exposure. Standard resuscitation principles (evaluation and management of airway, breathing, and circulation) should be followed in most cases, with the exception that supplemental oxygen should not be used in those with mild-to-moderate hypoxia since it causes reactive oxygen species to develop (ROS)20. Our patient had normal oxygen saturation at room air, therefore oxygen therapy was not given. As she had features of fluid deficit as evident by postural hypotension, fluid boluses (20 ml/kg over 15–30 min) were provided in the emergency room14. Activated charcoal (1 g/kg in water; maximum dose 50 g) or Fuller’s Earth (2 g/kg in water; maximum 150 g in water) is given as soon as possible per oral or via a nasogastric tube to patients who present early14. However, because she presented five days later, these treatments were not performed on her.

Although it has been shown that activated charcoal hemoperfusion reduces paraquat levels, there is insufficient evidence to establish a survival benefit in humans17,21. It is only effective if

![Figure 2. Patients tongue on twentieth day of paraquat ingestion during follow up visit to medicine outpatient department.](Image)

Table 1. Comparison of blood parameters on admission and on follow up.

<table>
<thead>
<tr>
<th>Blood parameters</th>
<th>Day 5 (at the time of admission)</th>
<th>Day 20 (at the time of first follow up visit)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urea</td>
<td>153</td>
<td>31</td>
</tr>
<tr>
<td>Creatinine</td>
<td>8.6</td>
<td>0.9</td>
</tr>
<tr>
<td>Sodium</td>
<td>128</td>
<td>140</td>
</tr>
<tr>
<td>Potassium</td>
<td>3.3</td>
<td>3.6</td>
</tr>
<tr>
<td>Total bilirubin</td>
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<td>0.4</td>
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<tr>
<td>AST</td>
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<td>21</td>
</tr>
<tr>
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<td>67</td>
<td>23</td>
</tr>
<tr>
<td>ALP</td>
<td>74</td>
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</tr>
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started within 4 hours of consumption, because peak paraquat concentration in the lungs takes 5–7 hours\(^1\). Hemodialysis is used to help people with acute renal failure, but it doesn’t accelerate drug clearance because the drug is quickly transported to the lungs and other organs\(^2\). In moderate-to-severe instances, immunosuppression with a combination of cyclophosphamide and methylprednisolone has been proven to be effective by preventing chronic inflammation\(^3\). Because oxygen-free radicals produced by peroxidation are the fundamental biochemical mechanism for lung injury, a range of antioxidant drugs have been studied to stop the process. Superoxide dismutase, vitamins C and E, N-acetylcysteine, desferrioxamine, and nitrous oxide have all been studied, but none have been proven to be effective\(^4\).

**Conclusion**

The amount of poison consumed and the time taken to receive medical treatment determines the prognosis. The high death rates are due to the toxicity of the substance as well as the lack of an antidote. Positive indications of prognosis include younger age, inhalation or percutaneous delivery, exposure to less paraquat, absence of acidosis, renal, hepatic, and pancreatic failures on admission\(^5\). The most common late sequelae among survivors include renal failure, esophageal erosions, esophagitis, and strictures. Progressive pulmonary fibrosis is another late result of paraquat poisoning, which can lead to death 2–3 weeks later owing to hypoxia and respiratory failure. As a result, patients with paraquat poisoning must be monitored for these late complications in the outpatient clinic on a frequent basis.

**Data availability**

All data underlying the results are available as part of the article and no additional source data are required.

**Case report consent**

Written informed consent for publication of their clinical details and clinical images was obtained from the patient. Ethical approval for this case report was not required.

**References**