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A 51-Year-Old Man with Icter, Oliguria and Epigastric Pain

Vahideh Mohammadzadeh (PhD)[1], Alireza Esmaeili (MD)[2], Bita Dadpour (MD)[3]*,

[1]*Faculty of Pharmacy, Mashhad University of Medical Sciences, Mashhad, Iran.*
[2]*Department of Emergency Medicine, Shahid Sadoughi University of Medical Sciences, Kerman, Iran.*
[3]*Medical Toxicology Research Center, School of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran.*

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ABSTRACT

Introduction: Paraquat poisoning through oral exposure is highly fatal and can lead function derangement in several organs and some special complications, such as pulmonary fibrosis.

Case Report: A middle-aged man was admitted to emergency unit in a regional hospital taking half a cup of herbicide in a suicidal attempt. He was completely alert and awake at the time of admission, complaining of epigastric pain. Vital signs were normal once admission in medical toxicology center in Mashhad and the urine sample was positive for paraquat. Hemodialysis was performed and continued due to the positive screening test, as well as rise of serum urea and creatinine and oliguria on the second day of hospitalization. An increase in bilirubin and transaminases was observed on the fifth day. Abdominal ultrasound image was normal. Respiratory distress developed on the fifth day and deteriorated over time until the 11th day. Cyclophosphamide and prednisolone were prescribed on day two after admission. The patient deceased after 13 days of hospitalization, despite all conservative treatments.

Conclusion: in case of paraquat poisoning, the rapid and timely performing techniques to limit toxin substance absorption from GI and blood might be lifesaving., hemodialysis (more available than other extra corporal removal techniques) at the earliest possible time (in the first minutes and hours), and continuing if necessary Is recommended. Physicians should be aware of the symptoms of paraquat toxicity, prognosis and treatment recommendations

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Introduction

Poisoning with pesticides and other agricultural chemicals is a major problem all over the world, in particular in developing countries. Around 20,000 deaths and more than 2 million hospitalizations annually have been reported due to poisoning with pesticides and agricultural chemicals. Paraquat is a nitrogenous herbicide that is environmentally hazardous and decomposes into non-toxic compounds after contact with soil. Although poisoning with this herbicide accounts for only 0.34% of all pesticide poisoning cases, it has the highest mortality rate (1).

The reported mortality from acute poisoning with paraquat herbicide varies from 33% to 78%. Oral intake of commercially available paraquat (20% concentration) is potentially

**Correspondence Author:* Medical Toxicology research Center, School of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran. Tel: +985138598973; Email: DadpourB@mums.ac.ir

fatal. Early death in patients with paraquat poisoning occurs as a result of vascular damage, while later mortality is due to acute lung injury (2).

A dose of 30 mg/kg of paraquat, equivalent to 7-8 milliliters of its commercial 24.6% solution, can be fatal. Paraquat can cause local irritation in the mouth, oropharynx and esophagus and damage several organs (kidney, heart, respiratory system, and liver). This toxicity leads to producing free radicals and oxidative stress that accompany cytotoxicity (3).

Immediate gastric lavage to reduce the absorption and activated charcoal to disable poison in the stomach are recommended. Three degrees of poisoning may be detected: (a) mild poisoning after intake or injection of less than 20 mg/kg body weight; in these cases, patients are asymptomatic or the symptoms are limited to the gastrointestinal system. All patients are fully recovered. (b) moderate to severe poisoning, usually after intake (rarely infused), is 20-40 mg/kg body weight. Non-specific signs of physical illness with local digestive symptoms before kidney failure (which may be self-healing) and pulmonary fibrosis, which may not be apparent for days or weeks.

Death occurs in most cases, but usually occures after 2-3 weeks. (c) acute poisoning is followed by the use of significant amounts of paraquat (greater than 40 mg/kg body weight). In addition to localized symptoms, multiple organ failures (heart, respiration, liver, kidney, and adrenal, pancreatic, nervous) occur. Death may occur within a few hours or be postponed in less than a few days (4).

Extracorporeal removal thecniques(ECRTs) are recommended (even for several days for prevention of rebound phenomenone) to reduce serum toxin level.

Blood purification along with enough and early gastrointestinal elimination should begin as early as possible; it has been recommended that blood purification be continued until clinical recovery along with negative urine test be obtained. (5). Prognosis is poor and dependent to carrying out immediate management (6). In this report we present a paraquat poisoned patient who different treatment options were

Case Report

A 51 Y.O man without history of any co-morbidity referred to emergency unit or a regional hospital about thirty minutes after taking half a cup of a green herbicide, his complaint was nausea and vomiting on admission. He was transferred to the emergency unit of Clinical Toxicology Department (CTD) of Imam Reza Academic Hospital (as a tertiary center), Mashhad about 12 hours later. Urine toxicology test was positive for paraquat, Surgery consultation was carried out for inserting a jugular catheter, and hemodialysis was done for about two and half hours, about 8 hours after surgery consult. Another consultation was also requested for caustic injury by paraquat on the GI system. Upper endoscopy was performed and circular scars were reported in all parts of the esophagus and in the fundus of stomach. The patient's vital signs in the first day of admission to the CTD were:

PR: 85/min, Systolic/Diastolic BP: 115/80 mmHg, RR: 14/min T: 37℃. Urine output was 2500 CC in 24 hours. He suffered from shortness of breath and heartburn (CXR is showed in figure 1).

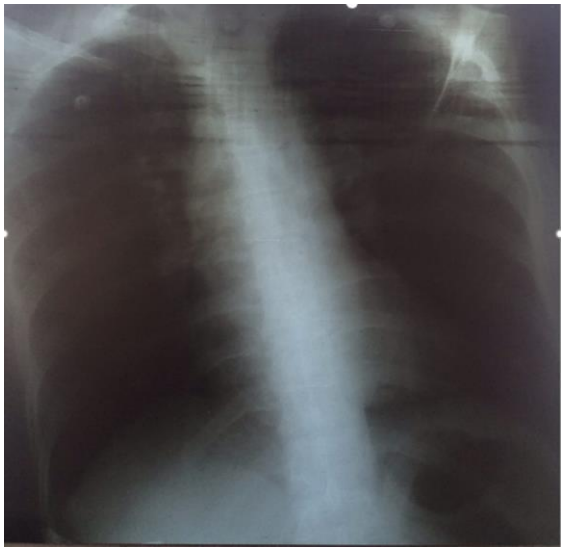

Figure 1: showed CXR on the first day

Infusion of cyclophosphamide at a dose of 370 mg/day as well as corticosteroid pulse injections (500 mg/day) were prescribed. Infusion of cyclophosphamide was continued for 3 days and methyl prednisolone pulse continued for2 days. The patient was receiving 370 mg Mesna at the same time. On the next day, the volume of urine reached

1000 CC in 24 hours and serum urea and creatinine raised to 107 mg/dl and 4.6 mg/dl respectively. The patient's skin gradually turned to yellow. Laboratory test results are presented in Table 1.

Table 1: Laboratory results on different days after admission tried to

	Day1	Day5	Day7	Day9	Day11	Day13
Arteriol blood gas						
Pao2 (mmHg)	41	19.4	21.2	46.9	46.6	34
Pco2 (mmHg)	30.1	29.2	31.8	24.7	86.2	43.3
Hco3 (meq/l)	21.4	16.4	18.4	16.5	21.1	21.4
PH	7.45	7.3	7.37	7.4	6.99	7.3
Biochemistry test						
Urea (mg/dl)	52	164	177	162	200	239
Cr (mg/dl)	1.7	5	4.9	6.2	6	6
SGPT (U/L)	12	381	729	117	_	117
SGOT (U/L)	22	272	242	_	_	71
Alp (U/L)	203	398	621	621	_	516
Na (meq/lit)	131	133	126	136	137	136
K (meq/lit)	3.4	3	2.6	3.8	3.9	4.3
Ca (mg/dl)	_	8.5	_	_	_	8.5
Bil.T (mg/dl)	_	7.8	11.6	20.2	25.6	24.2
Bil.D (mg/dl)	_	6.1	8.3	15.1	19.7	18.2
Alb (mg/dl)	_	3.3	_	2.8	_	2.6
Bs (mg/dl)	111	111	_	74	_	67
Blood count						
WBC (g/l)	11.300	3200	2600	1300	3100	5600
Hb (g/l)	12.1	9.1	10.6	9.1	5.3	7.9
Neut (g/l)	87.5%	_	_	_	_	_
Lym (g/l)	8.1%	_	_	_	_	_
Hct	36.8	_	_	_	_	_
Plt	175000	102000	152000	129000	138000	133000

Complete abdomen ultrasonography reported a normal liver size. There was no dilatation in the intrahepatic and extrahepatic bile ducts. He was dialyzed daily due to the positive result of urine paraquat. 6 days after hospitalization, urine paraquat test was negative, but hemodialysis continued due to acute kidney injury. Respiratory distress and decreased arterial oxygen saturation developed over 4 to 5 days of admission; he was intubated and underwent mechanical ventilation at day 5. On 11th day after admission, secretion of endotracheal tube was bloody. Coagulation tests were impaired. (PT: 29, PTT>180, INR: 2.1) Symptomatic treatment with FFP was initiated. CXR showed a pattern similar to that of lung edema. There was a possibility of alveolar hemorrhage (figure 2).

Despite frequent hemodialysis and treatment with immunosuppressive drugs and other supportive measures, including dexamethasone, N-acetyl cysteine, and vitamin E, unfortunately he deceased after 13 days of hospitalization.

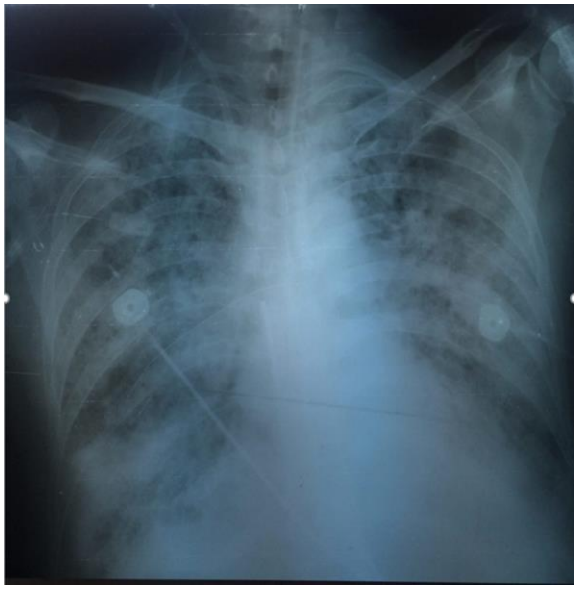

Figure 2: showed a pattern suggestive to pulmonary edema (hemorrhage)

Discussion

Paraquat is a herbicide from the bipyridyl group. It is considered to be one of the most toxic types of pesticides, so that 10 to 15 ml of 20% solution can lead to death. Although mortality is reported in the articles from 50 to 90 percent, it can be considered almost 100 percent, if someone has used it in a suicidal attempt. Paraquat's cytotoxicity is due to production of free radicals, which results in damage to the cell's lipid membrane and eventually destroys it. Lungs and kidneys are the most susceptible for damage by this poison. Acute pneumonitis and acute renal failure are two expected conditions caused by this poisoning, although mucosal injury due to local effects is usually the first patient's complaint. After consumption of equal or more than 20 ml of a 20% solution, the possibility of multiple organ injury is high, which includes respiratory failure, significant hypotension, acute kidney damage, liver damage, severe diarrhea and hemolytic anemia (7-9).

Diagnostic test is a qualitative urine test for paraquat. If test is negative after 6 hours of consumption and the patient is not symptomatic, the probability of significant injury is low, although the test should be repeated after 24 hours. Treatment is largely supportive. There are different opinions about using charcoal. In general, given that the toxin is absorbed very quickly from the GI system, the best time for administration of charcoal is within one hour of poison exposure. Nacetylcysteine, vitamin E and vitamin C are intended to reduce the oxidative stress in various articles, but its efficacy has not been proven. Immunosuppression drugs including cyclophosphamide along with corticosteroids have been recommended in recent years to reduce inflammation and subsequently the likelihood of its complications (e.g. lung fibrosis) although its effectiveness is now at issue. Pulse oximetry and chest radiography are recommended. Oxygen therapy is prescribed only if there is a significant hypoxemia, as this treatment can lead to more free radicals production and increased lung damage. . In the event of pain due to the caustic effects of poison on GI mucosa, intravenous injection of opioids (morphine) and use of local anesthetic (lidocaine) are recommended. Extracorporal removal methods, such as hemoperfusion and hemodialysis, might be particularly successful when are performed in the first few hours of exposure, which more amounts of poison still present in the circulatory system. Regular hemodialysis can be effective when paraquat serum concentration rebound occurs after hemodialysis. However, potential risks of extracorporal excretion methods should be considered including need for central venous access and electrolyte imbalance. According to previous studies, the most effective method for eliminating paraquat is hemoperfusion (32 ± 116 ml/min). However, hemoperfusion is expensive and probably ineffective if is performed after 6 hours of exposure. Hemodialysis (cleansing 54 ± 90 ml/min) and hemodia filtering are less efficient, but allowing for a longer duration of continuous removal (for 2 to 5 days or more). Hence, Hemofiltration is considered as the least effective treatment (6).

Since the major biochemical mechanism that causes damage to the lungs begins with oxygen free radicals produced by peroxidation, physicians are encouraged to use a number of antioxidant medications that may interfere with this process. Unfortunately, none of these treatments, including vitamin C and E, N-acetylcysteine, deferoxmine and nitrous oxide have been proven to be effective (10).

Despite all of the above measures, the prognosis is particularly weak in intentional

consumption. As in our patient, which presented almost all of the discussed symptoms, (developing respiratory failure, acute renal failure and liver dysfunction), despite frequent hemodialysis and treatment with immunesuppressive drugs and other supportive measures, including dexamethasone, N-acetyl cysteine, and vitamin E, unfortunately deceased after 13 days of hospitalization.

Conclusion

In case of poisoning with paraquat, the rapid and timely management, diminishing poison absorption techniques from GI and blood especially by hemo perfusion or hemodialysis, and continuing if necessary, along with other supportive therapies, can be the only way to save the patient's life.

No specific treatment has been defined and effectiveness of all proposed treatment options is on doubt.

We recommend that in the event of any pesticide poisoning which paraquat is suspected, urine paraquat be checked and prevention of gastrointestinal absorption be performed as soon as possible. If history strongly suggests paraquat poisoning or urine dithionite test is positive, the available extra corporal removal technique should be performed at the earliest possible time and repeated if necessary with close hemodynamic monitoring until negative urine test (if the initial urine test was positive) or clinical improvement be achieved.

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