

Outcome of Paraquat Self-poisoning a Case series

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Abstract: Introduction –Paraquat is available as 20% solution for agricultural purposes and deliberate ingestion can be lethal despite newer modalities of management. Methods - We present a case series from a tertiary care hospital, consisting of six patients admitted from January 2012 to December 2013 with history of paraquat ingestion. All of them were treated with supportive and specific care in the form of charcoal hemoperfusion (HP) and immunosuppression with cyclophosphamide and steroids and outcome was evaluated. Results - All patients developed respiratory, renal and hepatic dysfunction. Three patients died within one week of paraquat ingestion, two patients at the end of second week and one patient lost follow-up after discharge. Autopsy showed ARDS in three of them. Conclusion -Paraquat is highly toxic. Ingestion of concentrated form most likely results in non responsiveness to available modalities of treatment.

Keywords: Paraquat, Charcol hemoperfusion, Immunosuppressive therapy, ARDS, Renal and hepatic dysfunction

1. Introduction

Paraquat is a commonly used weedicide in Asia.^[1] It is a dipyridyl compound and a relatively safe agent as far as occupational exposure is concerned. But it is highly toxic when used for deliberate self harm and hence a major cause of pesticide death in developed and developing countries.^[2] Commercially produced 10-30% of concentrated forms are diluted and used for agricultural purposes. In weeds, it causes destruction of tissues on contact by inhibiting conversion of NADP to NADPH during photosynthesis.^[3] The latter causes formation of oxygen free radicals which destroy the lipid membrane of cell organelles leading to cell death.

Once ingested, paraquat is rapidly absorbed from gut, causing high blood levels from where tissue distribution and accumulation occurs,^[4] affecting mainly lungs, kidneys and liver. Absorption from stomach is incomplete; only 30% is absorbed and the remaining passes to intestine from where further continuous absorption can occur. 90% of absorbed poison is rapidly excreted through kidneys and which accumulated in viscera are excreted over days.^[5] Once tissue accumulation occurs, progressive tissue damage is likely.^[6] Paraquat can cause acute and late symptoms, both predominantly involving the respiratory system. In self poisoning where significant amount is ingested, symptoms

develop within hours to few days. Lung is the primary organ affected where it is maximally concentrated, followed by liver and kidney. It affects both type I and type II pneumocytes and death usually occurs due to ARDS. As it acts with oxygen molecules, resulting superoxide radicals can further destroy the lung tissue. In occupational exposure where minimal quantity is absorbed or deliberate poisoning where small quantity is ingested, symptoms are late to develop.

Acute tubular necrosis and fulminant hepatic failure are the other complications which augment the mortality.^[7] Direct cardiac toxicity and cardiogenic shock is also described. Multiorgan dysfunction commonly occurs causing death next to ARDS.

Though there are many treatment modalities recommended for paraquat exposure,^[8] the outcome remains poor.

2. Methods

We present a case series of six patients, consecutively admitted in medical wards with paraquat poisoning in a tertiary care hospital over a period of two years from January 2012 to December 2013. The diagnosis of paraquat ingestion was obtained from history, reference letters and the bottle produced. Treatment histories from other hospitals were obtained from reference letter.

In emergency department, patients were stabilized by securing airway, breathing and circulation. Oxygen supplementation was avoided as far as possible unless saturation fell below 70%.^[2] Activated charcoal was introduced through ryles tube to all patients and Fuller's earth whenever available.^[9] To remove absorbed poison from blood stream, charcoal hemoperfusion was given as early as possible and there after 24 hours. Immunosuppressive therapy in the form of 1gm cyclophosphamide for two days, 1gm methyl prednesolone for 3 days followed by 20 mg dexamethasone till recovery was given to modify tissue response.^[10] Patients were monitored for development of respiratory distress as

evidenced by tachypnoea or fall in oxygen saturation to below 90% and renal dysfunction as per KDIGO clinical practice guideline for acute kidney injury.^[11] Hepatic dysfunction was taken as more than double fold rise in transaminases. All patients received supportive measures including hemodialysis whenever necessary. Patients were followed up till recovery or death.

3. Case Series

The characteristics of patients are summarized in Table 1.

Table 1: Patient characteristics

Sl no.	Age / sex	Time to receive initial care	Time to receive specific care	Treatment received	Complications	Survival period	Autopsy findings
1	48/M	1 h	3.30 hours	FE [†] , CH ^{**} , IS [‡]	Multiorgan dysfunction at the time of presentation	1 day	Congested organs
2	26/M	30 min	6.40 hours	FE, CH, IS	Respiratory dysfunction on 7 th hour of consumption, hepatitis and renal dysfunction on 2 nd day	7 days	ARDS
3	40/F	3 d	4 days	FE, CH, IS	Respiratory, renal and hepatic dysfunction at the time of presentation	16 days	Congested organs
4	35/M	1 h	1 hour	FE, CH, IS	Hepatitis on 2 nd day, renal and respiratory dysfunction on 3 rd day	2 days	ARDS
5	31/M	3 h	10 hours	FE, CH, IS	Hepatitis and renal dysfunction on 2 nd day, respiratory distress on 4 th day	13 days	ARDS
6	54/F	3.15 h	3.15 hours	FE, CH, IS	Hepatitis on 2 nd day, renal and respiratory dysfunction on 3 rd day of consumption	Discharged against medical advice	NA

*Fuller's earth, **Charcol hemoperfusion, †Immunosuppressive therapy

Age of patients ranged from 26 to 54; four men and two women. Except one, all of them were referred from primary centers where they received initial symptomatic treatment. The exact amount of poison ingested could not be assessed and all gave history of taking at least one mouthful. Specific treatment was given in our institution, consisting of fuller's earth, charcoal hemoperfusion, steroid and cyclophosphamide. Notably, in spite of treatment, all developed renal, hepatic and respiratory dysfunction.

Soon after ingestion, all developed vomiting and burning sensation in mouth. Case 3 consumed one mouthful of poison and vomited immediately. She disclosed the history only on 3rd day when she developed breathlessness and at the time of admission, had renal, hepatic and respiratory dysfunction. Case 5 also gave history of vomiting soon after poison ingestion. Five of the patients expired and one patient was discharged against medical advice after developing respiratory distress. Survival period ranged from 24 hours to 16 days.

4. Discussion

As paraquat is highly toxic and by intuition, preventing absorption remains the only method to reduce toxicity and improving outcome.^{[2][12]} Ingestion of more than 40 mg of paraquat ion/kg body weight can lead to multiorgan failure

with acute renal failure, hepatic necrosis, myocardial necrosis, acute pneumonitis, internal haemorrhages, pulmonary fibrosis and finally death.^[13] Ingestion of less than 20-40 mg/Kg causes slow toxicity with development of oral, esophageal and gastric erosions in the first 24 hours, hepatocellular and acute kidney injury in the next 24 to 72 hours and pulmonary fibrosis in 72 to 96 hours.^[14] Depending upon the amount, development of symptoms may be delayed for days to weeks.

All the patients in our series had multi organ dysfunction despite receiving specific care within four hours in three of them. Paraquat toxicity depends on the blood level.^[7] Initial absorption occurs from stomach and intestine in first six hours- primary organ accumulated being lungs at this stage- prolonging upto 18 hours.^[9] Studies on animal models have shown that constant blood level is seen upto 30hrs, suggesting continuous absorption from intestine. Hence measures to prevent absorption from gut and removal from blood by extracorporeal elimination remain the methods for reducing toxicity, unlikely benefiting those with high amount of ingestion due to early extensive tissue damage. In our series, five patients received initial care within four hours (among which two received within one hour) but developed multiorgan dysfunction.

Adsorbents like activated charcoal, bentonite and fuller's earth might have a role in preventing further absorption from stomach and intestine especially given within six hours of

ingestion. Strongest adsorbent capacity is for fuller's earth, hence preferred, but others are also useful if this is not available.

Unlike hemodialysis, extracorporeal elimination with hemoperfusion effectively removes poison from blood if given within first six hours of poison ingestion,^{[15][16]} especially in the initial hours as evidenced by lesser blood levels in survivors. Single hemoperfusion can cause 99% reduction of the poison level in blood.^[17] Hemodialysis is considered as renal replacement therapy if acute tubular necrosis occurs. However, in our series, three patients who received hemoperfusion within four hours also had poor outcome, probably due to larger amount of ingested poison. Hsu et al analysed 207 patients with severe paraquat poisoning treated with charcoal hemoperfusion and observed that those received HP within 4 hours post ingestion had significantly reduced mortality.^[18]

Immunosuppressive therapies are found to be of questionable beneficial in few trials, especially in moderate to severe poisoning. Lin et al published a RCT in 1996 showing survival benefit in patients treated with steroid and cyclophosphamide when given as pulse dose for one or two days rather than high dose for 14 days.^[19] However, their role in fulminant cases is minimal as per previous studies. Later the same author published another RCT in 2006 showing the benefit of repeated pulses of cyclophosphamide whenever oxygen saturation falls below 60%.^[20] At the same time Perriens et al in another RCT showed no difference in survival benefit in those received supportive therapy or immunosuppressants.^[21]

Severity of poisoning is graded as mild, moderate to severe and fulminant retrospectively, usually reflecting the amount of poison ingested. In fulminant cases, death occurs in first week, aggressive therapies becoming futile. Here we had three patients with fulminant course and two with moderate to severe poisoning. Paraquat is available as 20% solution and an amount less than 5ml causes mild, of 5 to 15ml (half to 1.5 teaspoon) is sufficient to produce moderate to severe while more than 15ml is expected to produce fulminant poisoning.^{[22][23]}

Studies have shown that plasma paraquat levels can be used for assessing prognosis and accordingly various nomograms have been devised. Poor outcome is seen in patients with blood level of more than 5gm/L at any time. Proudfoot et al measured plasma paraquat level in 79 patients and correlated with outcome. Patients whose plasma concentrations do not exceed 2.0, 0.6, 0.3, 0.16, and 0.1 mg/l at 4, 6, 10, 16, and 24 h respectively are likely to have good outcome.^[24] Alternatively, calorimetric urine paraquat estimation (urine benzathionine test) also helps in prognostication. Urine colour change to dark or navy-blue has poor prognosis while light blue has got good prognosis.^{[25][26][27]} Liu et al observed 11 patients with paraquat poisoning and found out that plasma and urine paraquat levels were significantly low in survivors than non-survivors.^[28] Urine test can also be used for predicting fulminant cases before starting immunosuppressive therapy.

Occupational exposure of paraquat runs a milder course as paraquat is used indiluent form for agriculture purposes. A study on Srilankan workers have shown that despite evidence of dermal exposure of paraquat used for spraying, it was not detected in urine samples.^[29] Hence the production of paraquat in highly concentrated form may be discouraged.

5. Conclusion

Paraquat self poisoning carries extremely bad outcome in spite of early medical care- ingestion of even small quantities of concentrated paraquat (20%) can have severe to fulminant clinical course. Cause of death in acute toxicity remains hepatorenal dysfunction and ARDS.

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