



# ORIGINAL RESEARCH PAPER

## General Medicine

### PARAQUAT: A FATAL POISON

**KEY WORDS:** Paraquat, Poisoning, ARDS, AKI

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#### ABSTRACT

Paraquat is a toxic herbicidal poison. Exposure to even minimal dose can prove fatal. Unavailability of antidote makes management of these patients difficult, making it highly fatal compound. We present you a case series of 9 patients who had exposure of paraquat compound which had fatal outcome in majority of patients. 66.7 (n=6) were male and 33 % (n=33%) were female. The case fatality rate was 66.7% (n=6). More the quantity of the consumption higher the chances of the death was seen. Patients who survived consumed less than 15 ml of paraquat compound. Pulmonary involvement was seen in 55.5% (n=5) patients. With onset of pulmonary involvement, severe ARDS was seen within shorter time span of 6 to 12 hours. All the patients who had pulmonary involvement eventually succumbed. Renal involvement was seen in 66.7% (n=6) patients. The mean creatinine was 3.2 mg/dl. Among the patients with renal involvement (n=6), 3 patients died (50%). Hepatic involvement was seen in 1 patient.

#### INTRODUCTION

Paraquat (N, N-dimethyl-4, 4-bipyridinium dichloride; PQ), is herbicide used widely throughout our country. Cost effectiveness and easy availability makes its use more common<sup>[1]</sup>. Mild intoxication can cause minor gastrointestinal problems like vomiting, diarrhoea, oropharyngeal ulcerations. With severe intoxication there can be respiratory distress, pulmonary fibrosis, acute renal failure, multi-organ failure and eventually can lead to death<sup>[1, 2]</sup>. Highest concentration of Paraquat is found in the lungs<sup>[3, 4]</sup>. Unavailability of specific antidote, fatality remains high in patients of paraquat intoxication. Treatment modalities like gastric lavage, intentional diarrhoea, diuresis, and dialysis can be used in treatment of these patients<sup>[5]</sup>.

#### Case series

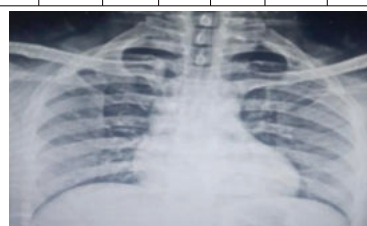
##### Case 1

A 32 year old male with consumption of 10 ml of paraquat compound was hospitalized within 4 hours of consumption. On admission patients pulse was 82 per minute, blood pressure of 120/70 mmHg and oxygen saturation of 98%. His chest x-ray was normal on admission. Patient was given gastric lavage, antioxidant, and hemo-dialysis therapy. There was gradual rise in levels of serum creatinine. He had serum creatinine of 4 mg/dl on day 4 of consumption. Total 3 sessions of hemo- dialysis were given to patient during his treatment. CT-KUB was suggestive of acute kidney injury. Patient was discharged on 10<sup>th</sup> days of admission. Patient didn't had any respiratory involvement during his course of treatment.

**Table 1 - showing relevant vital and laboratory parameters**

PARAMETER	DAY 1	DAY 2	DAY 3	DAY 4	DAY 5	DAY 6	DAY 7	DAY 8	DAY 10
Pulse rate (bpm)	112	102	134	128	112	104	100	98	102
Blood pressure (mmHg)	110/90	130/90	140/90	140/90	120/90	140/90	130/90	130/90	140/90
Oxygen saturation (%)	96	96	97	98	98	96	96	98	98
Haemoglobin (gm/dl)	10.7	11.7	10.6	11.6	11.4	11.8	10.6	10.1	12.3

Total leucocyte count (cu mm)	7.6	6.06	6.01	5.7	5.4	5.07	4.1	4.1	6.6
Serum creatinine (mg/dl)	6.1	4.54	2.77	1.55	1.5	1.9	1.4	1.13	1
Serum urea (mg/dl)	149	98	104	58	63	57	45	32	29
Urine output (ml/24 hours)	1200	800	600	90	1100	1400	1600	1800	2100



**Figure 1 – Chest X-ray PA view of case number 1 on admission**

##### Case 2

A 35 year male came with consumption of paraquat compound 6 hours prior to admission. The quantity of compound consumption was not known. Patient was vitally stable on admission with pulse rate of 76 per minute, blood pressure of 110/70 mmHg and oxygen saturation of 97%. His chest x-ray was clear on admission. The serum creatinine on admission was 0.8 mg/dl. There was sudden increase in serum creatinine on 2<sup>nd</sup> day to 2.9 mg/dl. Dialysis was initiated. Patient succumbed on day 5 of admission.

**Table 2-showing relevant vital and laboratory parameters**

PARAMETER	DAY-1	DAY-2	DAY-3
Pulse rate(bpm)	100	102	134
Blood pressure (mmHg)	130/90	130/90	140/90

Oxygen Saturation (%)	97	96	96
Haemoglobin (gm/dl)	14.1	13.8	14.8
Total leucocyte count (cu mm)	7.3	7.4	7.8
Serum creatinine (mg/dl)	0.8	1.7	2.9
Serum urea (mg/dl)	24	92	104
Urine output (ml/24 hours)	2500ml/24hrs	2000ml/24hrs	1200 ml/24hrs
Total bilirubin (mg/dl)	1.4	1.2	1.2



**Figure 2 – Chest X ray PA view of case number 2 on admission**

### Case 3

A 24 years female came with history of suicidal consumption of 50 ml of paraquat compound 6 hours prior to admission. Patient vitals on admission were pulse rate of 98 per minute, blood pressure of 110/70 mmHg and Oxygen saturation of 90 % on admission. Chest X-ray PA view on admission was showing haziness over bilateral lung fields. Patient didn't had any renal involvement throughout the hospital course. Her baseline creatinine was 1.1 on admission. Over the period of 24 hours she went into severe ARDS and was taken on BIPAP followed by mechanical ventilation. Patient succumbed after 24 hours of admission.

**Table 3-showing relevant vital and laboratory parameters**

PARAMETER	ON ADMISSION	06 HRS	18 HRS
Pulse rate (bpm)	108	106	112
Blood pressure(mmHg )	100/70	110/90	120/80
Oxygen saturation (%)	90 % ON room air	94% On BIPAP	90 % on mechanical
Haemoglobin (g/dl)	10.7		
Total leucocyte count (cu mm)	33.95		
Serum creatinine (mg/dl)	0.8		
Serum urea (mg/dl)	34		
Total bilirubin (mg/dl)	1.3		



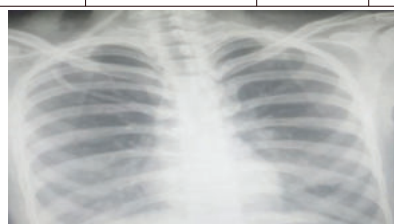
**Figure 3 – Chest X-ray PA view of case number 3 on admission showing bilateral lower zone haziness**

### Case4

A 60 years male came with history of suicidal consumption of 40 ml of paraquat compound 24 hours prior to admission. On admission his pulse rate was 130 per minute, blood pressure of 120/80 mmHg and oxygen saturation of 50 % with haziness on bilateral lung fields on chest x-ray. Patient also had a decreased urine output and creatinine of 7.4 mg/dl since admission. As patient was in severe ARDS, he was taken on mechanical ventilation. Patient succumbed within 12 hours of admission.

**Table 4-showing relevant vital and laboratory parameters**

PARAMETER	ON ADMISSION	06 HRS	12 HRS
Pulse rate (bpm)	130	80	112
Blood pressure(mmHg)	120/80	110/90	120/80
Oxygen saturation (%)	50 % On RA	94% On BIPAP	90 % on mechanical ventilation
Haemoglobin (g/dl)	16.2		
Total leucocyte count (cu mm)	2.93		
Serum creatinine (mg/dl)	7.3		
Serum urea (mg/dl)	185		
Total bilirubin (mg/dl)	5.6		



**Figure 4 – Chest X-ray PA view of case number 4 on admission**

### Case 4

A 24 year male came with suicidal consumption of 20 ml of paraquat compound 8 hours before hospitalization. On admission patients pulse rate was 112 per minute, blood pressure of 120/80 mmHg and oxygen saturation of 99 % Saturation. The serum creatinine was 0.9 mg/dl on admission. Within next 6 hours the oxygen saturation dropped to 80% and in next 4 hours patient went into severe ARDS and with saturation of 60% on NIV following which patient was intubated. The patient succumbed after 28 hours of hospitalization.

**Table 5-showing relevant vital and laboratory parameters**

PARAMETER	ON ADMISSION	12 HRS	24 HRS
Pulse rate (bpm)	112	126	140
Blood pressure(mmHg)	120/80	110/80	110/70
Oxygen saturation (%)	99 % On RA	77% On BIPAP	82% on mechanical ventilation
Haemoglobin (g/dl)	8.7		
Total leucocyte count (cu mm)	17.6		

Serum creatinine (mg/dl)	0.9		
Serum urea (mg/dl)	34		
Total bilirubin (mg/dl)	1.6		



**Figure 5 – Chest X-ray PA view of case number 5 on admission showing bilateral lower zone haziness**

#### Case 5

A 24 year male came with suicidal consumption of 2ml of paraquat 2 hours prior to hospitalization. He had pulse rate of 92 per minute, blood pressure of 120/80 mmHg and oxygen saturation of 97% on room air. The serum creatinine gradually increased from baseline of 1.16 to 3.6 mg/dl and then gradually decreased to 1.47mg/dl. He had acute kidney injury which was treated with diuretic therapy. He didn't had any respiratory involvement. His vital parameters were stable throughout the hospital course. He was discharged after 10 days.

**Table 6 - showing relevant vital and laboratory parameters**

PARAMETER	DAY-1	DAY-2	DAY-3	DAY-4	DAY-5	DAY-6	DAY-8	DAY-9
Pulse rate (bpm)	102	100	98	94	94	96	84	84
Blood pressure (mmHg)	130/80	130/80	120/90	120/80	120/80	130/90	120/90	120/80
Oxygen saturation (%)	97	97	97	98	98	98	98	98
Haemoglobin (g/dl)	15.2	15.4	15.4	15.4	14.7	14.8	14.6	14.6
Total leucocyte count (cu mm)	9.69	6.06	11.8	11.2	10.8	10.8	8.2	6.6
Serum creatinine (mg/dl)	1.16	1.24	3.21	3.04	3.60	2.8	1.5	1.47
Serum urea (mg/dl)	32	35	40	50	69	57	32	29
Urine output (ml/24 hours)	2200	2900	3000	2900	2800	2800	3000	2900
Total bilirubin (mg/dl)	1.2	1.9	1.3	1.3	1.5	1.4	1.5	1.4



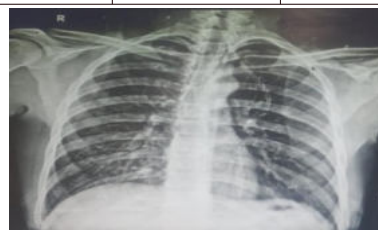
**Figure 6 – Chest X-ray PA view of case number 6 on admission**

#### Case 6

A 24 year female came with history of paraquat compound consumption of around 40ml 2 hours before the admission. The patient had a complaints of vomiting and breathlessness. His vitals on admission were pulse rate of 122 per minute, blood pressure of 130/70mmHg and oxygen saturation 80% on room air. Patient was intubated immediately in view of severe ARDS. Patient died after 4 hours of admission.

**Table 7-showing relevant vital and laboratory parameters**

PARAMETER	ON ADMISSION	2 hours
Pulse rate (bpm)	122	126
Blood pressure (mmHg)	130/70	110/60
Oxygen saturation (%)	80 % on room air	72% on Mechanical ventilation
Haemoglobin (g/dl)	15.9	
Total leucocyte count (cu mm)	38.95	
Serum creatinine (mg/dl)	1.47	
Serum urea (mg/dl)	27	
Total bilirubin (mg/dl)	1.2	



**Figure 7 – Chest X-ray PA view of case number 7 on admission**

#### Case 7

A 28 year male came with complaints of paraquat compound consumption about 2 ml 1 hour before hospitalization. The patients vitals on admission were pulse rate 102 per minute, blood pressure of 120/70 mmHg and oxygen saturation of 96% on room air. Patient was given symptomatic treatment and monitored for vitals and lab parameters. Patient didn't had any respiratory involvement during his course of treatment. The creatinine was gradually raised to a peak of 1.8 mg/dl on day 6 and then it decreased to 1.4mg/dl. Patient was discharged on day 8

**Table 8-showing relevant vital and laboratory parameters**

PARAMETER	DAY-1	DAY-2	DAY-3	DAY-4	DAY-5	DAY-6	DAY-7
Pulse rate (bpm)	102	92	90	90	84	86	86
Blood pressure (mmHg)	120/80	120/80	130/90	120/80	120/80	130/80	120/80
Oxygen saturation (%)	98	99	97	98	99	98	98
Haemoglobin (g/dl)	17.2	16.4	16.4	15.8	15.7	15.8	16.1
Total leucocyte count (cu mm)	7.87	8.06	10.5	11.2	9.8	9.8	8.4
Serum creatinine (mg/dl)	0.81	1.04	1.21	1.04	1.60	1.8	1.4
Serum urea (mg/dl)	21	24	32	30	29	37	24

Urine output (ml/24 hours)	1900	2500	2300	2200	2800	2500	2800
Total bilirubin (mg/dl)	1.2	1.5	1.6	1.3	1.4	1.4	1.5



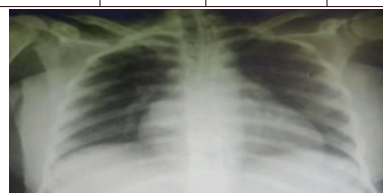
**Figure 8 – Chest X-ray PA view of case number 8 on admission**

### Case 8

An 18 year old female with 9 months of pregnancy came with complaints of paraquat compound consumption of around 15 ml, about 8 hours before the admission. Vitals on admission were pulse rate 102 per minute, blood pressure of 110/70 and oxygen saturation of 80 % on room air. The creatinine was on increasing trend, on day 3 serum creatinine was 4.1mg/dl. Spo2 was decreasing daily, on day 3 patient was intubated in view of severe ARDS. Patient succumbed on day 4 of hospitalization.

**Table 9-showing relevant vital and laboratory parameters**

PARAMETER	Day 1	Day 2	Day 3
Pulse rate (bpm)	122	118	124
Blood pressure(mmHg)	110/80	120/80	100/70
Oxygen saturation (%)	99 % On RA	79% On BIPAP	80 % on Mechanical ventilation
Haemoglobin (g/dl)	7.7	6.2	6.8
Total leucocyte count (cu mm)	20.6	23.4	22.8
Serum creatinine (mg/dl)	1.72	2.73	4.1
Serum urea (mg/dl)	19	45	84
Urine output (ml/24 hours)	800ml	600ml	250ml
Total bilirubin (mg/dl)	1.6	1.3	1.3



**Figure 9 – Chest X-ray PA view of case number 9 on admission**

**Table 10 - Summary**

Parameters	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7	Case 8	Case 9
Age/sex	32/M	35/M	24/F	60/M	24/M	24/M	24/F	28/M	18/F
Motive	Suicidal	Suicidal	Suicidal	Suicidal	Suicidal	Suicidal	Suicidal	Suicidal	Suicidal
Time of presentation	4hours	6hours	6hours	24hours	8hours	2hours	2hours	1hour	8hours

Amount of consumption	10 ml	Not known	50 ml	40 ml	20 ml	2 ml	40 ml	2 ml	15 ml
Kidney involvement	Present	Present	Absent	Present	Absent	Present	Absent	Present	Present
Peak serum creatinine	6.1	2.9	0.8	7.3	0.9	3.6	1.47	1.8	4.1
Lung involvement	Absent	Absent	Present	Present	Present	Absent	Present	Absent	Present
Liver involvement	Absent	Absent	Absent	Present	Absent	Absent	Absent	Absent	Absent
Peak serum bilirubin	1	1.4	1.3	5.6	1.6	1.9	1.2	1.6	1.6
Outcome	Survived	Death	Death	Death	Death	Survived	Death	Survived	Death

### Summary

Out of total 9 patients 66.7 (n=6) were male and 33 % (n=33%) were female. Male to female ratio was 2:1. Among 3 females 1 female was ANC case. The mean age of patients was 30 years. Youngest age was 18 years and oldest age was 60 years. The average length of hospital stay was 3.4 days, with shortest stay is about 12 hours and longest stay was 10 days. The case fatality rate was 66.7% (n=6).

The mode of exposure was by oral route in all the patients. More the quantity of the consumption higher the chances of the death was seen. In our study patients who survived consumed less than 15 ml of paraquat compound. The main symptoms and signs of paraquat poisoning were nausea, vomiting, epigastric pain, difficulty in swallowing, oral ulcerations, breathlessness and decreased urine output. Pulmonary involvement was seen in 55.5% (n=5) patients. The spo2 was gradually decreased over 6-12 hours and many patients were intubated within 24 hours of hospitalization. With onset of pulmonary involvement, severe ARDS was seen within shorter time span of 6 to 12 hours. All the patients who had pulmonary involvement eventually succumbed. Renal involvement was seen in 66.7% (n=6) patients. The mean creatinine was 3.2 mg/dl. Among the patients with renal involvement (n=6), 3 patients died (50%) and 3 patients survived (50%). Hepatic involvement was seen in 1 patient.

### DISCUSSION

Paraquat is an herbicidal agent is widely used throughout the country. Exposure to the paraquat is highly toxic for humans. On ingestion of paraquat compound there is local ulceration of mucosal surface. It gets rapidly absorbed from the gastrointestinal tract and distributed to the entire body. Highest concentration of paraquat is in lungs followed by kidneys. Involvement of heart, liver, central nervous system is not uncommon. Paraquat leads to generation of toxic reactive oxygen species through redox cycling<sup>[1]</sup>.

Mild intoxication can occur with dose less than 20mg/kg causing nausea, vomiting, oropharyngeal ulcerations, dysphagia and loose stools. Moderate intoxication can occur with dose between 20 to 50 mg/kg and patient can suffer from pulmonary fibrosis, acute kidney injury within 2 to 3 weeks. Severe intoxication of dose more than 50 mg/kg is highly fatal and lead to death due to severe ARDS and MODS within 3 days of intoxication<sup>[1-3]</sup>.

Diagnosis of paraquat poisoning can be done by urinary



paraquat concentration <sup>[1, 3, 4]</sup>. Levels less than 1mg/L in 24 hours of ingestion is suggestive of better outcome in patients of paraquat poisoning. Serum level of paraquat can also be used for diagnosis <sup>[1]</sup>.

Due to unavailability of antidote, treatment usually comprises of removal of unabsorbed compound by induction of vomiting, gastric lavage, loose stools and hemo-dialysis. Hemoperfusion with activated charcoal is effective if initiated within 4 hours of intoxication. <sup>[1, 4, 5, 6, 7]</sup>. Due to reactive oxygen species involved in pathology, judicious use of oxygen therapy is required. Oxygen therapy should only be used to correct hypoxemia <sup>[1]</sup>. N acetyl cysteine and vitamin c can be used as an antioxidant therapy which can help in scavenging reactive oxygen species and by increasing glutathione levels. Supportive treatment with opioid analgesics can help to decrease pain of mucosal ulceration <sup>[1,2]</sup>. Glucocorticoids and cyclophosphamide can also be used as an immune modulators to decrease organ damage caused by reactive oxygen species <sup>[1]</sup>.

Early use of hemodialysis can decrease progression and help in rapid recovery <sup>[6,7]</sup>. Delayed use of hemodialysis has not proven to have mortality benefit in patients due to deposition of paraquat in the tissues <sup>[7]</sup>.

## CONCLUSION

It can be concluded from above mentioned case series that paraquat is a highly toxic compound. Even minimal dose can lead to severe clinical outcome. Urinary paraquat level remains a highly specific diagnostic test. Early initiation of hemodialysis i.e. within 4 hours of consumption can have a better prognosis. Mortality rates remains high due to unavailability of specific antidote. Hence measures to restrict the use of paraquat compound can help to decrease morbidity and mortality occurring due to paraquat compound.

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