Trends in Clinical and Medical Sciences

PSR Press

Article

Paraquat-induced acute kidney injury in hospitalized patients in western orissa: clinical profile and long-term outcome

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Received: 1 April 2023; Accepted: 15 May 2023; Published: 24 May 2023.

Abstract: Due to the lack of effective therapies, therapeutic care such as medicines and early hemodialysis is viewed as the major kind of supportive care for paraquat poisoning. The aim of our present study was to evaluate acute kidney injury and its impact on various clinical parameters, including length of hospital stay, episodes of hemodialysis, number of ICU admissions, and mortality rates. This prospective observational study was launched after receiving approval from the Institutional Ethics Committee. All patients with acute renal injury caused by paraquat were admitted to the ward of the Department of General Medicine, VIMSAR, Burla, and included in the present study after obtaining informed written consent from each participant. The results showed that serum phosphorus and uric acid were highly significant ($P < 0.001$) when compared to laboratory features based on clinical outcomes, followed by alanine aminotransferase (ALP; $P = 0.006$), serum bicarbonate ($P = 0.007$), and serum potassium ($P = 0.009$). In conclusion, paraquat poisoning has no cure, but clinicians can monitor vital statistics and laboratory changes from diagnosis onward to understand the disease's trajectory. It is recommended that the government prohibit the widespread distribution of this pesticide and inform the public about its toxicity.

Keywords: Paraquat; Superoxide radicals; NADPH; Liver failure; Renal failure; Paraquat-induced acute kidney failure.

1. Introduction

To get rid of unwanted plants, farmers use chemicals known as herbicides. Paraquat, or 1, r-Dimethyl-4, 4-bipyridinum dichloride, is a syrupy liquid used to reduce weeds and grass in agricultural fields [1]. Poisoning from paraquat can occur whether the plant is consumed on purpose or by accident. However, intentional poisoning is on the rise due to its ease of access [2]. An increase in suicides in western Odisha has prompted serious health concerns related to the most widely used herbicide, paraquat.

It's rapidly partially absorbed, and then mostly flushed out in the urine, with very little metabolization. Extremely high mortality occurs even with minimal consumption [2]. When an antioxidant is used, it is absorbed and then concentrates inside many cells, where it undergoes redox cycling and generates reactive oxygen species such superoxide radicals that deplete cellular NADPH and damage cells. Paraquat poisoning causes several organ dysfunctions, including respiratory distress, renal failure, liver failure, and heart failure. Other side effects include mild irritation of the mouth, oropharynx, and esophagus.

Due to the lack of effective therapies, therapeutic care, such as medicines and early hemodialysis, is viewed as the major kind of supportive care and could reverse paraquat poisoning. Hence, our present study was to evaluate acute kidney injury and outcome by length of hospital stay, effect and episodes of hemodialysis, number of ICU admission and mortality.

2. Material and methods

This prospective observational study was launched after receiving approval from the Institutional Ethics Committee. All patients with acute renal injury caused by paraquat were admitted to the ward of the

Department of General Medicine, VIMSAR, Burla were included in the present study after taking informed written consent from each of the participant. The current study included as many patients as possible, with a minimum of 100 participants. Tools include a bed head ticket, a clinical examination kit, a sphygmomanometer, laboratory investigation reports, evidence of poisoning (a bottle and a picture), a 5 ml syringe, a needle, sample collection vials, and a pulse oximeter. Interview approach, clinical examination, and assessment of test findings are some of the techniques used.

The demographic details on the population were duly recorded. Consumption amounts, poisoning triggers, and time elapsed before hospitalization were meticulously documented. An extensive evaluation, tests, and follow-up were all part of the hospital stay. An entire blood count, hemoglobin percentage (in an EDTA-containing vial), total bilirubin, indirect bilirubin, aspartate transaminase (AST), alanine transaminase (ALT), alkaline phosphatase (ALP), urea, creatinine, uric acid, serum phosphate, and serum electrolytes all require a separate blood draw. Arterial blood gas analysis was performed. All samples are forwarded to the VIMSAR Regional Diagnostic Center, where accurate data is promptly gathered.

2.1. Statistical analysis

Standardized data collecting forms were used to capture information, and SPSS was used for analysis. Frequencies and percentages were used to represent qualitative data. Mean plus standard deviation was the method of presentation for numerical data. We tested the effects of several variables using Chi-squared. If the p-value is less than 0.05, the result is reliable.

3. Results

Statistical analysis was used to determine the relationship between demographic and clinical factors and clinical outcomes in paraquat-induced acute kidney injury (PQ-AKI) cases. It was discovered that no criteria were significant for the clinical outcome. However, the above research revealed some clinical associations that should be considered when dealing with similar patients in the future. The death pattern was seen to be higher throughout all age categories, i.e., 25, 25-35, 35-45, 45-60, and > 60 years, with a maximum mortality rate of 83.3% in the 25-35 and 35-45 years of age groups, which had a comparable distribution in numbers. On the contrary, the discharge rate is higher among cases under the age of 25, followed by cases between the ages of 25 and 35, and finally cases between the ages of 35 and 45. Absence among cases was shown to follow a similar trend to discharge. In terms of gender engagement, it was discovered that males were more likely than females to be involved in PQ-AKI. It is also noticed that female mortality rates are higher than male mortality rates [58 (77.3%) vs. 23 (88.5%)]. While, in terms of getting discharged or getting absconded from hospital, male patients outnumbered the female patients respectively [i.e., absconded: male versus female (10 (13.3%) vs. 3 (11.5%))]. Interestingly, all the female cases either absconded or died. There were no female patients discharged from the hospital who had been hospitalized with PQ-AKI. [i.e., discharged: males (7 (09.3%) vs. females 00 (00.0%] When considering the time between poison consumption and hospitalization, it was discovered that if the time is less than 12 hours, patients are more likely to be discharged from the hospital than if the time is greater than 12 hours. However, if the interval between paraquat consumption and hospitalization exceeds 36 hours, the death risk among all patients stays at 100%. Furthermore, a mean average volume of 31.7424.65 ml exacerbates the 100% death probability in paraquat ingested patients. However, in terms of clinical result, the length of stay among cases did not demonstrate any correlation with the severity of the condition, (Table 1).

Table 1. Patient features and clinical outcomes in paraquat-induced acute kidney injury.

Variables	Outcome			
	Discharge	Absconder	Death	P value
Age (in years)	<25 years	3 (12.5%)	4 (16.7%)	0.335
	(25-35) years	2 (5.6%)	4 (11.1%)	
	(35-45) years	1 (4.2%)	3 (12.5%)	
	(45-60) years	0 (0.0%)	2 (13.3%)	
	>60 years	1 (50.0%)	0 (0.0%)	
Gender	Male	7 (9.3%)	10 (13.3%)	0.250
	Female	0 (0.0%)	3 (11.5%)	
Amount of poison	9.86±4.91	29.77±18.39	31.74±24.65	0.062
Time between ingestion and hospitalization	<12 hrs.	7 (12.1%)	8 (13.8%)	0.339
	(12-24) hrs.	0 (0.0%)	3 (14.3%)	
	(24-36) hrs.	0 (0.0%)	2 (25.0%)	
	(36-48) hrs.	0 (0.0%)	0 (0.0%)	
	>48 hrs.	0 (0.0%)	0 (0.0%)	
Length of stay	8.86±3.67	6.77±2.42	8.20±2.94	0.205

According to the results of the above analysis, decreased urination (0.5 ml/kg/hr) was found to be statistically significant (P0.001). It was also discovered that mortality was frequent across all metrics, and the percentage of released patients with the conditions was relatively low. Shortness of breath (SOB) and crepitation both had statistically significant p-values of 0.027 and 0.036, respectively. Parameters that are not statistically significant may be regarded clinically useful (Table 2).

Table 2. Correlation of clinical characteristics based on clinical outcomes.

Variables	Outcome			
	Discharge	Absconder	Death	P value
Decreased urination (<0.5 ml/kg/hr)	Present	2 (2.2%)	12 (13.3%)	<0.001
	Absent	5 (45.5%)	1 (9.1%)	
Oral ulcer	Present	6 (6.6%)	11 (12.1%)	0.848
	Absent	1 (10.0%)	2 (20.0%)	
Chest pain	Present	0 (0.0%)	1 (8.3%)	0.614
	Absent	7 (7.9%)	12 (13.5%)	
Shortness of breath (SOB)	Yes	0 (0.0%)	6 (12.2%)	0.027
	No	7 (13.5%)	7 (13.5%)	
Crepitations	Present	0 (0.0%)	7 (14.9%)	0.036
	Absent	7 (13.0%)	6 (11.1%)	
Pedal edema	Present	1 (1.8%)	6 (10.7%)	0.052
	Absent	6 (13.3%)	7 (15.6%)	

In Table 3, laboratory parameters based on clinical outcomes in the present study participants were shown. The Serum phosphorus and uric acid were shown to be highly significant (P 0.001) when compared to the laboratory features based on clinical outcomes, followed by alanine aminotransferase (ALP; P = 0.006), serum bicarbonate (P = 0.007), and serum potassium (P = 0.009).

Table 3. Laboratory parameters based on clinical outcomes

S. No	Variables	Outcome			
		Discharge	Absconder	Death	P value
1	Total leukocyte count (TLC)	8631.43±2111.01	9666.54±3771.97	11706.79±4787.27	0.101
2	Hemoglobin (HB)	12.54±1.71	12.63±1.06	12.28±1.48	0.670
3	Total platelet count (TPC)	3.61±1.13	3.05±1.18	3.33±1.16	0.556
4	C-reactive protein (CRP)	10.29±7.91	20.38±15.60	26.43±17.05	0.032
5	Serum urea	109.71±21.99	151.23±50.79	146.23±42.63	0.084
6	Serum creatinine	1.19±0.42	1.51±0.29	1.72±0.70	0.082
7	Serum sodium (Na)	138.14±5.15	135.85±8.70	136.01±7.74	0.775
8	Serum potassium (K)	3.79±0.34	3.35±0.65	4.02±0.76	0.009
9	Serum calcium	1.33±0.40	1.19±0.25	1.32±0.29	0.328
10	Serum phosphorus (P)	2.91±0.42	4.00±0.87	4.26±0.77	<0.001
11	Serum uric acid	4.29±0.71	6.98±2.08	7.06±1.65	<0.001
12	Serum Bicarbonate (HCO3)	22.43±3.05	20.92±3.17	19.23±2.90	0.007
13	Total bilirubin	1.73±0.43	4.87±3.18	4.26±2.67	0.036
14	Direct bilirubin	0.73±0.26	2.41±1.74	2.02±1.61	0.071
15	Alanine transaminase (ALT)	55.86±27.85	104.46±50.17	96.93±53.04	0.106
16	Aspartate transaminase (AST)	49.29±21.09	94.08±49.61	91.56±57.72	0.147
17	Alkaline phosphatase (ALP)	165.00±92.02	370.85±176.54	324.77±132.37	0.006

4. Discussion

Our analysis found that men outnumbered women in their 20s and 30s. This matches Sarkar TS. et al.'s clinic epidemiological study and Mood NE. et al.'s cross-sectional study [3,4]. It could be psychological issues with men agricultural workers having better access to this chemical than women. Seok SJ. et al. found that males were more poisoned than females. The author investigated why men have more paraquat poisoning and didn't research the attempted suicide's cause. Suicide attempts are said to be caused by family problems, economic challenges, pessimism, and despair. Many categories overlap. An economic crisis may cause family issues, pessimism, and depression, which has been linked to a high number of poisoned suicide attempts [5].

In their Odisha cross-sectional study, Sarkar TS. et al. discovered that farming caused most paraquat toxicity in India. Odisha reached similar conclusions. The Public Health Care Centre, VIMSAR, Burla has seen the most paraquat poisoning cases since 2017. Paraquat instances were greater in western Odisha, Jharkhand, and Chhattisgarh. The state has 157 paraquat poisoning instances since 2017. The cause is unknown. Our research revealed most cases in western Odisha, indicating a comparable prevalence. Farmers have easier access to paraquat, which may explain the higher prevalence in the west [3,6].

Paraquat consumption and hospitalization time after intake were the main predictors of death. Liu HL. et al. found that people who survived 72 hours were younger and drank less paraquat [1.5 3.4 mg/mL vs. 54.0 97.4 mg/mL, p 0.001] [7]. Our study indicated that patients who arrived at the hospital in less than 12 hours had the best survival rate, which gradually fell. Age also affected PQ-AKI mortality. Our study found that younger patients had higher survival rates. Our study also indicated that an average mean amount of 31.7424.65 mg/ml increased hospitalized patient mortality. Paraquat poisoning severity and prognosis depend on dose. However, determining the amount is often impossible. In a clinical study of 41 cases of paraquat poisoning, Delirrad M. et al. found that 25 ml or fewer was associated with a good outcome [8].[4,6] Afzali S. et al. think 10–20 mL of a 20% solution is lethal [9]. [65] Amiri AH. et al. found that paraquat patients die at 20 ml. [66] Hospitalization length did not affect illness prognosis. Gil HW. et al. noted that it depended on paraquat intake [10]. [6,7] Due to lack of research, such links are hard to determine.

Kim SJ. et al. found 34.7% of patients failed and only 10 incidences of oliguric AKI [11]. [6,8] In a case report, Ito H. et al. found that PQ-AKI causes silent acute renal impairment, decreased urination, and fluid resuscitation [12]. [6,9] Yadla M. et al. observed 60 PQ-AKI cases in Hyderabad, India, in a comprehensive retrospective study. Vomiting, mouth ulcers, and stomach pain were the most prevalent symptoms. 26% of patients had oliguric AKI. 95% needed renal replacement treatment. 38 (68%) of sixty patients died [13]. Acute paraquat exposure causes AKI for many reasons. Song Y. et al. found that mouth ulcers independently increase paraquat-induced AKI risk. Oral paraquat poisoning damages oral and esophageal mucosa, causing ulcers and

burning. Mouth ulcers may indicate the severity of oral paraquat exposure. The mouth ulcer severity matches the ailment. Oral ulcers make paraquat overdose more fatal. In children with acute paraquat exposure and oral ulcers, clinicians should evaluate AKI [14]. Urination, shortness of breath, crepitation, and pedal oedema decreased statistically. Oral ulcers were not statistically significant, but they were clinically significant since they were more common in hospital admissions.

Weng CH. and Delirrad M. [15] found a statistically significant connection between admission service and outcome (P=0.009). Critically ill patients with ARDS symptoms or who need intensive care must be moved to the ICU. ICU patients have a high mortality risk [8,15]. This matches our findings. ICU hospitalization increased death in most cases. The PQ's nephrotoxic activity and clinical presentation that affects renal and lung function may be to blame [15].

Serum phosphorus and serum uric acid were highly statistically significant (P0.001), followed by ALP, serum bicarbonate, and SR K. Jung SY. et al. found a positive connection between phosphorus levels and AKI severity. AKI patients have hyperphosphatemia. It's likely due to poor phosphate clearance and renal function-induced secondary hyperparathyroidism. Hyperphosphatemia in CKD patients has been heavily stressed [16,17]. Kim JH. et al. found a similar result using prediction score for serum uric acid in PQ-AKI. Hyperuricemia was associated with a greater death rate (68.4% vs. 38.3%, P 0.05). AKI was 64.3% and renal failure 43.3%. Hyperuricemia increased the chance of death and kidney failure by 3.7 and 3.3 times, respectively, after correcting for age, gender, and expected paraquat intake. The mortality and renal failure groups exhibited greater mean serum uric acid concentrations than the survival and non-AKI groups. The blood uric acid level after acute paraquat poisoning may be a useful clinical diagnostic for diagnosing death and AKI risk [18]. ALP and serum potassium are positively correlated, like our findings [17].

Few studies found paraquat-induced death in functional markers as serum creatinine [15,19]. In a retrospective cross-sectional study, Gheshlaghi F. et al. found that paraquat use significantly increased creatinine and death risk. The dead had minor ALT and AST increases. When serum paraquat levels are unavailable, creatinine levels on different days after an overdose may indicate toxicity [20]. Our analysis anticipated that dying patients had a higher mean creatinine level than discharged patients (7.251.38 vs. 4.662.02). Creatinine elevations after paraquat exposure may compromise renal function, according to Mohamed F. et al. In response to acute oxidative stress, creatine and creatinine production increases to fulfill energy demands, causing serum creatinine to rise rapidly. Acidosis increases creatine-to-creatinine cyclisation and inhibits creatinine release. After paraquat poisoning, creatinine does not indicate renal functional loss. Renal damage to biomarkers should be more specific. Estimating PQ-AKI severity is difficult because the pathophysiology is unknown [21].

PQ-induced AKI treatment is controversial. No therapy has been effective. Traditional hemodialysis (HD) removes paraquat and reduces acute renal impairment in many settings. Its usefulness is disputed. paraquat poisoning mortality prevention research is ongoing. HD did not improve patient survival in a thorough investigation and meta-analysis by Eizadi-Mood N. The severity of the poisoning, the amount of paraquat taken, the period between paraquat administration and HD, and the length and timing of HD sessions may affect mortality. Our study found a positive HD outcome connection [22].

Radiological results in PQ-AKI cases were usually lung-related. This disease caused lung, liver, and kidney abnormalities. Respiratory failure raised mortality. Im JG. et al. examined 42 paraquat users with abnormal chest x-rays. Radiographs showed widespread consolidation, pneumomediastinum with or without pneumothorax, cardiomegaly, and superior mediastinum enlargement in the first week after ingestion. The most prevalent parenchymal abnormality at 2-4 weeks was small linear and cystic shadows. Localized honeycombing was the main parenchymal abnormality at 4 weeks. A high-resolution lung CT nine months after paraquat exposure showed localized fibrosis with tiny cysts. Thus, paraquat poisoning causes air space consolidation and lung fibrosis in the final stage [23]. Our study showed that CXR and HRCT s/o fibrosis were statistically significant. Our investigation found increased paraquat-related sepsis and hepatopathy deaths. Sepsis was not statistically significant, although both indications potentially indicate AKI severity.

5. Conclusion

Although there is currently no cure for paraquat poisoning, doctors can gain insight into the disease's course by monitoring vital parameters and dynamic changes in laboratory measures from the time of diagnosis

onward. In addition, the government should take the necessary steps to prevent this pesticide from becoming more readily accessible and available to the public, and the public should be made aware of its toxicity through suitable channels. In addition, it is vital to highlight that paraquat poisoning is highly lethal, and there is no known antidote. Individuals should avoid contact with paraquat, employ protective measures when handling herbicides, and follow recent safety guidelines supplied by regulatory agencies and product manufacturers.

Author Contributions: All authors contributed equally to the writing of this paper. All authors read and approved the final manuscript.

Conflicts of Interest: The authors declare that they do not have any conflict of interests.

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