ISSN: 0975-3583,0976-2833 VOL15, ISSUE 04, 2024

LUNG INVOLVEMENT IN PARAQUAT POISONING: UNRAVELLING THE COMPLEX WEB

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Received Date: 17/03/2024 Acceptance Date: 17/04/2024

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Abstract

Background: Paraquat, a widely used herbicide known for its efficacy in weed control, has gained notoriety for its potential toxicity to humans. The current study examines the manifestations, consequences, and course of paraquat intoxication.

Methodology: At our tertiary care center, 10 cases of paraquat poisoning were recorded during the course of the study, which lasted a full year. In our study, all cases included purposeful ingestion, meaning the patient attempted suicide. Out of ten patients, only one patient survived. This suggests that patients who present early (4 hours) and with less ingestion have a higher chance of surviving.

Conclusion: Among the various systemic effects associated with paraquat poisoning, lung involvement stands out as a critical and often fatal manifestation. According to our study, pulmonary fibrosis, Respiratory failure and ultimately multi-organ failure are the most frequent consequences that result in mortality. This article explores the intricacies of lung complications arising from paraquat exposure, shedding light on the underlying mechanisms, clinical presentation, diagnostic challenges, and potential therapeutic interventions.

Keywords: Paraquat, Respiratory failure, Pulmonary fibrosis

Introduction

Paraquat (1,1'-dimethyl-4,4'-bipyridinium dichloride) has been employed globally in agriculture for decades due to its potent herbicidal properties. Despite its widespread use, paraquat has become a significant public health concern, primarily due to its high toxicity and the lack of a specific antidote. One of the most devastating consequences of paraquat poisoning is its impact on the respiratory system, with lung involvement being a prominent and life-threatening complication.

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Methodology

The present study includes the data of Ten patients of paraquat poisoning over 1 year. Analysis of data was performed and presented in a descriptive pattern.

Inclusion Criteria

1. Patients with history of Paraquat poisoning presented to asram general hospital

2. Age > 18 years

Case reviews

The ten cases of paraquat poisoning treated in Asram medical college and general Hospital from October 2023 to march 2024 are summarised in Table 1. Most of the patients were young males (7) around the age 20-35 years, (1) 65 Yr old male and remaining (2) females in the age group of 30-40 years.

The length of hospital stay ranged from 1 to 28 days and eight of the ten patients died during hospitalisation. All cases had paraquat solution ingested for suicidal attempt. The concentration of paraquat solution ingested were not documented. one case had exposure to large amounts (400 ml). He developed pulmonary complications and died within 48 hours of admission.

Case 1 who ingested 5-10 ml of paraquat died even after immunosuppressive and anti-oxidant therapies. He presented to us on Day 18. He developed

Acute respiratory failure and was started on Hemoperfusion at the time of admission and continued throughout the hospital stay. Steroid (methyl prednisolone 1 gram) and Cyclophosphomide were given. He developed acute interstitial pneumonitis and type 1 respiratory failure and was on mechanical ventilator with least PaO2/FiO2 value of 104 and subsequently died.

The patients in cases 2,8,9,10 consumed 15-20 ml of paraquat and presented with acute renal failure with a serum creatinine of more than 7mg/dl and acute hepatic failure with a serum bilirubin of more than 7mg/dl.They developed respiratory failure and was put on mechanical ventilator. They deteriorated even with steroids, cyclophosphamide,N-Acetyl Cysteine and Hemodialysis.

case 6 and 7 consumed 10-25 ml of paraquat and presented with shortness of breath and oral ulcerations. They developed acute renal failure and developed respiratory failure and subsequently died

Case 5 is a 68 Year old male ingested 400 ml and presented on Day 1 with severe nausea, vomitings and oral ulcerations. He developed respiratory failure and subsequently died with in 48 hours of admission

Case 4 is a 24 Year old male ingested 5ml of paraquat and started early on steroids, cyclophosphamide, N- acetyl cysteine and hemodialysis. He survived and was on hemodialysis twice in a month

Mechanisms of lung injury

Upon ingestion, paraquat accumulates in the lungs, exerts its toxic effects primarily through redox cycling, leading to the generation of reactive oxygen species (ROS). This oxidative

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 04, 2024

stress damages cellular structures and initiates a cascade of events, ultimately resulting in widespread inflammation and fibrosis within the lung tissue.

High doses of PQ (greater than 50 to 100 ml of liquid concentrate (20%)) have been shown to cause fulminant organ failure, as well as pulmonary edema, cardiac, renal, and hepatic injury, as well as CNS toxicity. These effects can cause convulsions, hypoxia, shock, and metabolic acidosis, and ultimately result in death from multi-organ failure within a few hours to a few days[1]. Less PQ typically has negative effects on developing kidneys and lungs over the course of the following two to six days[1].

Three categories of different clinical manifestations can be identified based on the amount of PQ ingested: Mild poisoning (less than 20 mg PQ ion per kg body weight (bw)), which causes gastrointestinal symptoms and may progress to renal damage, though full recovery is still possible; and severe poisoning (20–40 mg PQ ion per kg bw), which results in acute renal failure, acute lung injury, and advanced pulmonary fibroses, which leads to respiratory failure. Fulminant poisoning (greater than 40 mg PQ ion per kg bw = 20 ml of 20–24% concentrate), which involved multiple organ failure and ultimately led to all patients' deaths within hours to a few days after the PQ ingestion, may occur two to three weeks after PQ ingestion, though most patients could still recover[2]. Humans have been shown to have a fatal dose (LD50) of PQ of 20–40 mg ion per kg of body weight, or 1.2–2.4 US teaspoons of a PQ product with a 30% concentration[3]. Although the precise amount of PQ ingested in the cases presented has not been established, humans may be exposed to PQ through a variety of ways, with varying clinical manifestations and levels of toxicity anticipated in patients. Thus, more clinical research that takes into account varying PQ dosages should be planned.

Table 1 Case summary of Paraquat Poisoning from march 2023 to march 2024

PARTICULARS	**CASE 1**	**CASE 2**	**CASE 3**	**CASE 4**	**CASE 5**	**CASE 6**	**CASE 7**	**CASE 8**	**CASE 9**	**CASE 10**
AGE/SEX	20Y/M	22Y/M	28Y/M	24Y/M	68Y/M	25Y/M	34Y/M	22Y/M	33Y/M	38Y/M
Quantity Ingested (ml)	5-10ml	15-20ml	20ml	5ml	400ml	25 ml	10ml	15ml	15ml	10-15ml
Intent of consumption	SUICIDE	SUICIDE	SUICIDE	SUICIDE	SUICIDE	SUICIDE	SUICIDE	SUICIDE	SUICIDE	SUICIDE
Time Of Presentation	Day 18	Day 9	10 Hours	3 Hours	14 Hours	Day 5	Day 4	Day 7	Day 4	17 Hours
Presentation complaints	Shortness of breath, Fever, cough with	shortness of breath, decreased urine	Nausea, vomiting, diffuse abdomi	shortness of breath, Itching	Nausea, Vomitings	Shortness of breath, cough with scanty expec	ulcerations over tongue and palate	Shortness of breath, Decreased urine output, cough with expectoration	Oral ulcerations, difficulty in swallowing,throat pain,sh	2-3 episodes of vomitings, loose

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	scanty, mucoid expectoration	output	nal pain			toration, nausea			ortness of breath.	stools
Complications	Respiratory Failure	MODS	Gastritis	Renal failure	Gastritis	AKI	AKI	MODS,AKI,Hepatitis	Acute Liver Injury, Acute kidney injury	MODS, AKI
Serum Creatinine (mg/dl)	1.4	7.1	1.1	0.9	2.0	2.2	2.4	7.8	9.5	8.7
Serum Bilirubin (mg/dl)	1.1	12	1.4	1	1.6	1.0	1.1	7.4	13.5	13.4
Lowest PAO2/ FIO2 Value	104	98	352	326	208	75	209	138	190	210
Mechanical Ventilation	Yes	Yes	No	No	Yes	Yes	No	Yes	Yes	Yes
Renal Replacement Therapy	6 cycles HD	7 cycles HD	Nil	5 Cycles HD	1 Cycle HD	Nil	3 Cycles HD	6 Cycles HD	7 Cycles HD	6 Cycles
ICU Stay	12 Days	14Days	3 Days	7 Days	2 Days	6 Days	4 Days	11 Days	13 Days	10 Days
Total length of hospital stay	12 Days	14Days	3 Days	15 Days	2 Days	6 Days	4 Days	11 Days	13 Days	10 Days
Survival	Death	Death	LAMA	survived	Death	Death	Death	Death	Death	Death

Clinical Presentation

Patients with paraquat poisoning often present with a spectrum of respiratory symptoms, ranging from mild dyspnea to severe respiratory distress. Clinical manifestations includes

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fever, sialorrhoea, pupil mydriasis, oral and lip burn, body pain, weakness, lethargy, oral canker sores, painful lesions, tongue and throat redness, jaundice, dyspnea, bilateral crackles, crepitation, orrales, tachypnea, and discomfort in the mouth and throat. Acute pancreatitis and epilepsy can also be brought on by consuming 20 milliliters of PQ (20 percent W/V), a condition linked to free radicals or oxygen species created by PQ[4]. When roughly 100 milliliters of PQ (60% solution) concentration are accidentally consumed, symptoms such as nausea, vomiting, and a severe burning feeling in the substernum are suggested[5].

After consuming a modest amount of wine containing PQ, a 15-year-old girl experienced nausea, vomiting, pain, and neutropenia[6]. Likewise, a substantial increase was observed in 10 symptoms following PQ exposure, which included cough, diarrhea, eye irritation, headache, nausea, rhinitis, throat irritation, breathing difficulties, unusual weariness, and wheezing[7]. In addition, pediatric patients who experienced PQ poisoning also reported experiencing hepatitis (66.7%), shock (50.0%), hypoxemia (33.3%), respiratory failure (33.3%), abdominal pain (33.3%), acute renal failure (33.3%), gastrointestinal tract bleeding (33.3%), nausea/vomiting (16.7%), and seizures (16.7%)[8]. When individuals purposefully consumed PQ, they acquired acute non-oliguric renal failure, oral mucosa ulcers, and acute liver damage. After four hours, one of these patients made it to the hospital, but sadly, not before passing away from basic supportive care[9]. These clinical characteristics illustrated how PQ can have fatal consequences for the heart, liver, kidney, lungs, gastrointestinal system, and other organs. Therefore, during PQ intoxication, clinical signs should be observed in addition to odor perception since they aid in the primary diagnosis of PQ poisoning.The onset of symptoms is typically rapid, occurring within hours of exposure. Radiological examinations, such as chest X-rays and CT scans, may reveal patterns consistent with pulmonary edema, consolidation, and fibrosis.

Diagnostic Challenges

Diagnosing lung involvement in paraquat poisoning poses significant challenges, primarily due to the absence of specific biomarkers and the rapid progression of symptoms. Paraquat poisoning was diagnosed in our patients based on history of ingestion and strong supporting physical examination findings, including oropharyngeal burns and the development of acute kidney injury, metabolic acidosis, and toxic hepatitis afterward.
Tests on the urine or blood may be performed to validate the diagnosis.
It has been established that a plasma concentration of more over 1.6 pg/ml twelve hours after ingestion is universally deadly[10]. The prognosis has been established as well as the diagnosis confirmed by the presence of paraquat in the urine. However, because these tests are not accessible in our center, they were not conducted on our patient.

Treatment Strategies

The management of paraquat-induced lung injury remains a formidable task for healthcare professionals. Current therapeutic interventions focus on minimizing further absorption, enhancing elimination, and attenuating oxidative stress.

Nasogastric tube fixation, charcoal-sorbitol lavage, gastric lavage with normal saline, forced alkalinized diuresis, and hemodialysis or hemoperfusion are all part of the conventional treatment. If hemoperfusion with activated charcoal is started within four hours of becoming intoxicated with paraquat, it is beneficial. Benefits were not anticipated for our patients as none of them reported witthin 4 hours[11]. The accumulation of paraquat in lung tissues causes hypoxemia, which necessitates the use of mechanical ventilation. Ironically, because it produces more harmful radicals, oxygen supplementation might have a negative impact.

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Therefore, oxygen should only be used to treat hypoxemia[12]. Antibiotics for supervening infections and hemodialysis or filtration to support renal function are examples of subsequent therapy. Strong painkillers, including opiates, might be needed to relieve severe pain brought on by inflammation, ulceration, and damage to the gastrointestinal tract. Certain antioxidants, such as vitamins C and E, have been utilized in medicine to guard against the harmful effects of free radicals. Because N-acetyl cysteine can enhance intracellular glutathione levels and scavenge free radicals, it is also employed as an antioxidant. As a result, it will give lung parenchymal cells protection[13-14].

A study by Lin *et al.* revealed a 75% survival rate when high doses of cyclophosphamide and glucocorticoids were used as a therapeutic intervention[15]. Agarwal *et al.*'s meta-analysis and study on intensive care units indicated that immunosuppressive therapy using glucocorticoids and cyclophosphamide may be useful in treating moderate-to-severe paraquat poisoning[16-17]. Various methods have been tested for supportive management of paraquat poisoning since there isn't a definite evidence-based treatment for it. However, despite aggressive treatment, the prognosis is often poor, emphasizing the critical need for preventive measures and improved therapeutic strategies.

Preventive Measures

Given the lack of a specific antidote and the high mortality associated with paraquat poisoning, prevention becomes paramount. Regulatory measures, such as restricted access to paraquat, stringent safety guidelines for handling, and public awareness campaigns, can play a pivotal role in minimizing the incidence of poisoning.

Conclusion

Lung involvement in paraquat poisoning represents a complex interplay of oxidative stress, inflammation, and fibrosis. Understanding the mechanisms underlying respiratory complications is crucial for developing targeted therapeutic approaches. The survival rate is high for patients who arrive at the emergency room (ER) within 6–8 hours following paraquat intoxication. Higher survival rates correspond with lower paraquat intake (20 mg/kg). No specific remedy is known to exist. In addition to other supportive measures, the combination of immunosuppression and antioxidant therapy is the key to managing patients with paraquat toxicity. The most frequent side effects of paraquat poisoning are hepatitis, oesophagitis, oropharyngeal ulcers, respiratory failure, acute kidney damage, and, in severe cases, circulatory collapse, multiple organ failure, and death.

As the scientific community strives to unravel the mysteries surrounding paraquat toxicity, a comprehensive strategy encompassing prevention, early detection, and innovative treatment modalities is essential to mitigate the devastating impact of lung involvement in paraquat poisoning.

References

1. I. B. Gawarammana and N. A. Buckley, Medical management of paraquat ingestion, Br. J. Clin. Pharmacol., 2011, 5, 745–757.
2. A. M. Sabzghabaee, N. Eizadi-Mood, K. Montazeri, A. Yaraghi and M. Golabi, Fatality in Paraquat poisoning, Singapore Med. J., 2010, 6, 496–500.
3. J. A. Vale, T. J. Meredith and B. M. Buckley, Paraquat poisoning: clinical features and immediate general management, Hum. Toxicol., 1987, 6, 41–47.
4. H. Dong, X. Peng and Z. Qiu, A rare case of epilepsy and acute pancreatitis induced by severe Paraquat poisoning, Ann. Transl. Med., 2017, 7, 163.

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5. M. A. Davarpanah, F. Hosseinzadeh and S. S. Mohammadi, Treatment Following Intoxication With Lethal Dose of Paraquat: A Case Report and Review of Literature, Iran Red Crescent. Med. J., 2015, 10, e19373.
6. N. Papanikolaou, G. Paspatis, A. Dermitzakis, E. Tzortzakakis, E. Charalambous and A. M. Tsatsakis, Neutropenia induced by paraquat poisoning, Hum. Exp. Toxicol., 2001, 11, 597–599.
7. R. G. Ames, R. A. Howd and L. Doherty, Community exposure to a paraquat drift, Arch. Environ. Health, 1993, 1, 47–52.
8. Y. W. Hsieh, J. L. Lin, S. Y. Lee, C. H. Weng, H. Y. Yang, 32. S. H. Liu, I. K. Wang, C. C. Liang, C. T. Chang and T. H. Yen, Paraquat poisoning in pediatric patients, Pediatr. Emerg. Care, 2013, 4, 487–491.
9. D. P. Olson, J. A. Diaz and J. D. Jereda, A fatal case of paraquat ingestion: clinical course and review of pathophysiology, Med. Sci. Monit., 2010, 12, CS153–CS156.
10. Gil H W, Kang M S,Yang J O, Lee, Hong S Y. Association between plasma paraquat level and outcome of paraquat poisoning in 375 paraquat poisoning patients. Clin Toxicol. 2008; 46:515–8.
11. Sandhu JS, Dhiman A, Mahajan R, Sandhu P. Outcome of paraquat poisoning - a five year study. Indian J Nephrol 2003;13:64-8.
12. Arts J, Schuit G, Schipper A, Kleij van der B. A case report of paraquat poisoning. Eur J Hosp Pharm 2006;12:22-4.
13. Dinis-Oliveira RJ, Duarte JA, Sánchez-Navarro A, Remião F, Bastos ML, Carvalho F. Paraquat poisonings: Mechanisms of lung toxicity, clinical features, and treatment. Crit Rev Toxicol 2008;38:13-71.
14. Dinis-Oliveira RJ, Sarmento A, Reis P, Amaro A, Remiao F, Bastos ML, *et al.* Acute paraquat poisoning: Report of a survival case following intake of a potential lethal dose. Pediatr Emerg Care 2006;22:537-40
15. Afzali S, Gholyaf M. The Effectiveness of Combined Treatment with Methylprednisolone and Cyclophosphamide in Oral Paraquat Poisoning. Arch Iranian Med 2008;11:387-91.
16. Agarwal R, Srinivas R, Aggarwal AN, Gupta D. Experience with paraquat poisoning in a respiratory intensive care unit in North India. Singapore Med J 2006;47:1033-7.
17. Agarwal R, Srinivas R, Aggarwal AN, Gupta D. Immunosuppressive therapy in lung injury due to Paraquat poisoning: A meta-analysis. Singapore Med J 2007;48:1000-5.