Original Research Article

A STUDY ON CLINICAL PROFILE AND OUTCOME OF PARAQUAT POISONING.

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Abstract:

Introduction: Paraquat (PQ, 1,1′-dimethyl-4,4′-bipyridinium) is a commonly used herbicide in India. PQ induces multi-organ failure involving lung, gastrointestinal tract, pancreas, kidney, liver, heart, and brain injury. Case fatality is between 40–60% and death usually occurs within 24–72 hours of ingestion in severe poisoning. Hence, this study was undertaken to study the clinical features and outcome following PQ poisoning. To understand various predictors of outcome and severity in relation to SOFA score**.**

Methodology: A prospective observational study was done in 50 patients of either sex admitted to a tertiary care with history of paraquat poisoning for a period of 2 years after obtaining institutional ethical committee clearance and patients informed consent. Detailed General Physical and Systemic Examination is carried out. All the patients who were hospitalized underwent the following tests: renal function test, liver function test, prothrombin time, arterial blood gas analysis, chest X-ray. Severity of poisoning is then assessed in relation to SOFA scores and other lab data. Data analysed using SPSS version 22 with $P<0.05$ considered as statistically significant.

Results: Majority belonged to the age group of 20-50years (68%), followed by > 50 years (20%) and < 20 years (12%). Males were 60% and females were 40%. Complications included metabolic acidosis in 20%, acute Kidney Injury in 64% and acute Lung Injury in 20%. Only 60% of patients survived. Mean SOFA score of patients who required mechanical ventilation, haemodialysis and who died was significantly high when compared to patients not on need of mechanical ventilation, haemodialysis and alive patients.

Conclusions: Paraquat poisoning can cause leucocytosis, thrombocytopenia and increased CRP levels. It causes AKI, ALI, ARDS, METABOLIC ACIDOSIS and MODS. SOFA SCORE can be used as a

prognostic factor and it can predict the development of AKI, ARDS, need for Mechanical ventilation and Haemodialysis.

Keywords: Paraquat poisoning, SOFA score, Clinical profile, outcome, tertiary care.

Introduction:

Paraquat (PQ, 1,1′-dimethyl-4,4′-bipyridinium) is a commonly used herbicide in India. [1,2, 3] Suicides due to paraquat (PQ) are an important cause of morbidity and mortality, especially due to the absence of specific antidote. Although there is no specific antidote, most patients receive steroids/cyclophosphamide/antioxidants to reduce free radical damage [1]. Metabolism of PQ generates free radicals that damage the cellular organelles and membranes, causing damage to many organs, especially the pulmonary alveolar epithelium.[4] PQ induces multi-organ failure involving lung, gastrointestinal tract, pancreas, kidney, liver, heart, and brain injury [5,6]. Consumption of PQ > 40 mg/kg causes acute multiorgan failure with death within the first 2 days, while < 20 mg/kg of PQ causes mild symptoms and most survive [7]. Paraquat of 20–40 mg/kg causes severe mucosal damage followed by multiorgan failure. The few, who survive, die within 2–4 weeks due to lung fibrosis. The pulmonary alveolar cells selectively accumulate polyamines that are required for cellular functions. Being structurally similar to polyamines, PQ gets accumulated in these cells, causing selective delayed lung injury [8]. Case fatality is between 40–60% and death usually occurs within 24–72 hours of ingestion in severe poisoning [4].

Inspite of its adverse effects, it is still widely used in many parts of the world. There is no awareness among the general population regarding its toxicity. It is classified as a Highly Hazardous substance in USA and is banned from usage in view of accidental or intentional exposure. Data on PQ poisoning are restricted to case reports and small case series. Hence, this study was undertaken to study the clinical features and outcome following PQ poisoning. To understand various predictors of outcome and severity in relation to SOFA score.

Methodology: A prospective observational study was done in all patients of either sex admitted to a tertiary care with history of paraquat poisoning for a period of 2 years after obtaining institutional ethical committee clearance and patients informed consent. Patients exposed to other poisonings, any previous history of lung disease, any previous history of liver disease, any previous history of kidney disease, any malignancy and those who did not give consent were excluded. Study was done in 50 patients all patients were included.

Patients with history of paraquat poisoning were examined. Detailed history is taken regarding the amount of poison consumed, the concentration of the poison, time elapsed from ingestion/exposure to hospital admission. Detailed General Physical and Systemic Examination is carried out. All the patients who were hospitalized underwent the following tests: renal function test, liver function test, prothrombin time, arterial blood gas analysis, chest X-ray. Severity of poisoning is then assessed in relation to SOFA scores and other lab data.

All the paraquat poisoning patients received treatment with 1g/kg of activated charcoal through the nasogastric tube following gastric lavage with normal saline in the emergency triage. Renal function test and liver function test were repeated every alternate day after starting therapy. Haemodialysis was initiated in needed patients. Patients who had abnormal renal function test i.e., serum creatinine > 2 mg/dl, abnormal liver function test i.e., alanine transaminase (ALT) > 80U/L and/or International Normalized Ratio (INR) > 1.5 were defined as having multiorgan failure. Patients who had PaO2 < 70

mmHg by arterial blood gas analysis at room air were defined as having acute lung injury secondary to paraquat poisoning

Results: Majority belonged to the age group of 20-50years (68%), followed by > 50 years (20%) and < 20 years (12%). With mean age 36.8 and range 17 – 55 years. Males were 60% and females were 40%. Amount consumed was 10-20 ml in 42% of patients. Patients who were admitted in a time frame of 12-24hrs were 44%, > 24hrs were 38% and <12hrs were 18%. Duration of hospital stay was 0 – 48hours in 40%, 48-96 hours in 16% and >96 hours in 44%. Complications included metabolic acidosis in 20%, acute Kidney Injury in 64% and acute Lung Injury in 20%. Only 60% of patients survived. (table 1)

Table 1: Distribution by various variables.

PARAMETERS	Sub- group	Frequency	Percentage
Age in years	< 20 years	6	12
	20– 50 years	34	68
	>50 years	10	20
Age (years) Mean±SD/ range		36.88 ± 11.6 years/ 17-55 years	
Sex	Male	30	60
	Female	20	40
Amount consumed	5 – 10 ml	15	30
	11-20 ml	21	42
	>20ml	14	28
Time from paraquat consumption to arrival at hospital (in hours)	<12	9	18
	12 - 24	22	44
	>24	19	38
Duration of hospital stay	0 – 48hours	20	40
	48-96 hours	8	16
	>96 hours	22	44
Complications	Metabolic acidosis	10	20
	AKI	32	64
	ALI	20	40
	Multiple Organ damage	19	38
Outcome	Dead	20	40
	Survived	30	60

ABG analysis on admission of patients with respect to mortality shows that PH, PO2, PCO2 and HCO3 of patients who were dead were significantly more compared with alive patients. Though PaO2/FiO2more in patients who were dead was slightly more when compared to patients who were alive it was not significant statistically. (table 2)

Table 2: Relationship of Biochemical Parameters on admission with Mortality

Biochemical Parameters	**Dead**		**Survived**		Independent t test P value
	Mean	**SD**	**Mean**	**SD**	
PH	7.20	0.68	7.82	1.043	0.02
PO2	89.55	7.44	96.56	1.30	<0.001
PCO2	40.60	4.40	36.63	2.57	0.0002
HCO3	22.40	3.06	24.46	1.75	0.004
PaO2/FiO2	352.89	10.76	349.54	13.65	0.36

Mean of neutrophil count was significantly high and mean of hemoglobin was significantly low in patients who died when compared to patients who survived. The difference seen in other haematological parameters in dead and survived patients was not significant statistically. (table 3)

Table 3: Relationship of Hematological Parameters on admission with Mortality

Hematological Parameters	**Dead**		**Survived**		**P Value***
	Mean	**SD**	**Mean**	**SD**	
Neutrophils	6600	2327.29	3876.67	1542.87	0.0001
Lymphocytes	2660	1027.20	2420.00	97.79	0.207
Platelets	2.23	0.81	2.50	0.91	0.2887
Hb	10.48	1.52	11.56	1.69	0.025
BUN	17.80	8.70	20.03	8.86	0.384
Sr.Creatinine	1.52	0.71	1.37	0.55	0.4048
Sr.Bilirubin	1.39	1.01	1.28	0.57	0.627
CRP	4.61	0.91	4.59	0.73	0.932
MAP	83.10	7.23	86.20	8.80	0.197

***Independent t test**

There was no significant difference in proportion of patients dead or survived with amount of paraquat poison consumed. (table 4)

Table 4: Amount consumed versus mortality

Amount consumed(ml)	**Dead N(%)**	**Survived N(%)**	**Total**	**P value***
5-10	7(46.66)	8(53.33)	15(100)	0.87
5-20	8(38.09)	13(61.91)	21(100)	
>20	6(42.86)	8(52.14)	14(100)	
Total	**20(40)**	**30(60)**	**50(100)**	

Mean SOFA score of patients who required mechanical ventilation, haemodialysis and who died was significantly high when compared to patients not on need of mechanical ventilation, haemodialysis and alive patients. (table 5)

Table 5: SOFA at various clinical situations and management

Variables	**Sub**	**SOFA Mean**	**SOFA SD**	**P value**

	group			
on admission	Alive	5.88	5.83	0.873
	Dead	5.66	2.29	
Mechanical ventilation at 48 hrs	Yes	7.91	1.37	<0.001
	No	3.94	1.34	
Haemodialysis at 48 hours	Yes	6.09	2.42	0.031
	No	4	1.51	
Outcome	Dead	10.75	6.65	<0.0001
	Alive	2.63	1.09	

Discussion:

Paraquat is easily available & inexpensive in many developing countries. Intentional ingestion is the major reason associated with paraquat poisoning and the mortality rate still remains very high. The clinical profile, laboratory investigations, prognostic factors of paraquat poisoning were studied.

In this study, the paraquat poisoning was most prevalent {68% of patients were} in the age group of 20 to 50 years, 20% of patients belonged to age group above 50 years with mean age 36.8 and range 17 – 55 years. In study by Ravichandran et al, median age was 28 years [1]. In a study by Jagadeesham M et al median age of the patients was 28.5 years [9]. In study by Raghavendra rao et al, the mean age of the paraquat poisoned patients was 26±7.679 years with a median age of 26 years [10]. Thus, young age group consumed paraquat due to their impulsive nature. This study throws light on the target age group so that it guides in management protocol and decreasing the mortality.

In this study, 60 % of the study subjects were male and the rest 20 % were female. In study by Ravichandran et al most of them were males (65.4%) [1]. In a study by Jagadeesham M et al 80% of the paraquat poisoned patients were males [9]. In study by Raghavendra rao et al, approximately, 65% of the paraquat poisoned patients were males and 35% were females [10]. In Southern part of India, males are actively involved in spraying fertilizers and pest.

In this study, 30% of patients consumed less than 10ml and 28% consumed more than 20ml. In study by Ravichandran many patients (54.5%) presented by 6–12 hours after ingestion of PQ and 54.5% had consumed moderate amount of PQ [1]. The complications were high in patients who consumed larger amounts of paraquat. The need for mechanical ventilation and haemodialysis was also increased in the group who consumed more amount.

The SOFA Score was also high in patients who died, and this demonstrates that amount consumed is an independent and most important factor for the outcome of these patients. According to Narcisse Elenga et al 2018, the severity and outcome was determined primarily by the amount of paraquat ingested [11]. The study has demonstrated increased mortality among patients who have consumed larger amounts.

In this study mortality was 40%, which was less when compared to study by Rao et al, of the 101 patients studied by Rao et al., the mortality rate was 61.4% [12].Study by Ravichandran et al stated that acute lung and renal involvement led to high mortality rate of 72.5%, with at least three more dying after discharge due to delayed lung fibrosis[1].Study by Narendra et al, Pavan et al, Banday et al, Jagadeesan et al and Prasad et al found mortality rate as 75%, 66.7%, 75%, 100% and 83.3% respectively [13,14,15,9,12].

In this study, only 18 % of the patients have arrived in the hospital within 12 hours after exposure to poison. And the majority of the patients arrived 24 hrs after the consumption of the poison. According to the study conducted by Cheng-Hao Weng et al 2017, multivariate logistic regression indicated that a longer time to hospital arrival ($P < 0.001$) was a poor prognostic factor. This highlights the importance of creating awareness among people for immediate healthcare, as early hospitalisation might improve the outcome [18]. However, this factor was not identified as an independent factor in this study because of differences in the amount consumed between the patients.

About 84% of the patients included in the study had developed acute renal failure. About 20 patients had expired within 48 hours even after haemodialysis. Also 30% of the patients had developed ARDS and were on mechanical ventilation and expired in 48 hours. According to the articles published by Gawarammana IB et al paraquat gets rapidly distributed with the highest concentration found in the lungs and kidneys [4]. This study also has demonstrated that patients with high SOFA scores had ARDS and were on mechanical ventilation.

The values of pH, paO2, PCO2 and Hco3- were low in patients who has consumed larger amounts of paraquat and in those who were deceased. Majority of the patients had metabolic acidosis secondary to AKI. This suggests that paraquat causes hypoxemia with acidosis.

The PCO2, HCO3- values in deceased patients were significantly lower than those in surviving patients in a study conducted by Changbao Huang et al in 2011. The study demonstrated that paraquat poisoning causes Leucocytosis. Leucocytosis is seen acutely in response to an inflammatory stressor/cytokine cascade.

In this study at Admission, the SOFA score was high (5 to 21) in 14 patients and all these patients did not survive after 48 hours. Also SOFA Score was high among patients who has consumed larger amounts of paraquat. At 48 hours, 12 patients needed mechanical ventilation in view of severe hypoxia and these patients had high SOFA score. At 48 hours, 22 patients with high SOFA score needed HD, Whereas the rest 8 patients were managed conservatively. And at 7 days, 10 patients were alive and 2 of them had high SOFA score, who recovered after haemodialysis. The 80% of patients who were deceased had high SOFA scores.

According to the study conducted by Wen Jie Wang et al results showed that higher SOFA in patients with PQ poisoning was related to severe mortality [19]. This suggests that SOFA SCORE can be used as a prognostic factor.

Conclusions: Paraquat poisoning can cause leucocytosis, thrombocytopenia, increased CRP levels. Patients had developed AKI, ALI, ARDS, METABOLIC ACIDOSIS and MODS. SOFA score can be used as a prognostic factor and it can predict the development of AKI, ARDS, need for Mechanical ventilation and Haemodialysis. In spite of haemodialysis, pulse therapy with steroids, antioxidant therapy and mechanical ventilation the mortality was still high. Therefore, reliable predictors of prognosis may be helpful to guide the treatment and future clinical research on antidotes and other therapy. Increased awareness among the clinicians and availability of the laboratory diagnostic methods might help to improve the outcome in at least a few patients. In spite of the extensive research and studies available in the literature, there is no curative treatment available for Paraquat poisoning. Hence measures should be taken to prevent the consumption or exposure to people. Hence, restricting the usage and availability of paraquat and banning this herbicide is the only curative approach available so far.

References:

1. Ravichandran R, Amalnath D, Shaha KK, Srinivas BH. Paraquat Poisoning: A Retrospective Study of 55 Patients From a Tertiary Care Center in Southern India. Indian J Crit Care Med. 2020 Mar;24(3):155-159.
2. Gunnell D, Eddleston M, Philips MR, Konradsen F. The global distribution of fatal pesticide self-poisoning: systematic review. BMC Public Health. 2007; 7:357.
3. Kumar D. Conditions of Paraquat use in India. [[Accessed 1st August 2019]]. http://www.iuf.org/w/sites/default/files/Joint%20paraquat%20study%20India_0.pdf Available from: [Ref list]
4. Gawarammana IB, Buckley NA. Medical management of paraquat ingestion. Br J Clin Pharmacol. 2011;72(5):745–757.
5. Sandhu JS, Dhiman A, Mahajan R, Sandhu P. Outcome of paraquat poisoning - a five year study. Indian J Nephrol. 2003; 13:64–68.
6. Li A, Li W, Hao F, Wang H. Early stage blood purification for paraquat poisoning: A multicenter retrospective study. Blood Purif. 2016;42(2):93–99.
7. Dinis-Oliveira RJ, Duarte JA, Sanchez-Navarro A, Remiao F, Bastos ML, Carvalho F. Paraquat poisonings: mechanisms of lung toxicity, clinical features, and treatment. Crit Rev Toxicol. 2008;38(1):13–71.
8. Hoet PH, Nemery B. Polyamines in the lung: polyamine uptake and polyamine-linked pathological or toxicological conditions. Am J Physiol Lung Cell Mol Physiol. 2000;278(3): L417–L433.
9. Jagadeesan M, Nithyananthan P, Banupriya M, Mahendrakumar K, Karthik PS, Kannan R. A study on clinical profile of paraquat poisoning in a tertiary care hospital. Int J Adv Med 2017; 4:1088-91.
10. Rao R, Bhat R, Pathadka S, Chenji SK, Dsouza S. Golden Hours in Severe Paraquat Poisoning-The Role of Early Haemoperfusion Therapy. J Clin Diagn Res. 2017 Feb;11(2): OC06-OC08.
11. Elenga N, Merlin C, Le Guern R, et al. Clinical features and prognosis of paraquat poisoning in French Guiana: a review of 62 cases. Medicine 2018; 97:e9621. Doi:10.1097/MD.0000000000009621pmid:http://www.ncbi.nlm.nih.gov/pubmed/29642226.
12. Rao R, Bhat R, Pathadka S, Chenji SK, Dsouza S. Golden hours in severe paraquat poisoning-the role of early haemoperfusion therapy. J Clin Diag Res. 2017;11(2): OC06.
13. Narendra SS, Vinaykumar. S. Paraquat poisoning: a case series in South India. Int J Sci Res. 2015;4(1):561–564.
14. Pavan M. Acute kidney injury following paraquat poisoning in india. Iran J Kidney Dis. 2013;7(1):64–66.
15. Banday TH, Bhat SB, Bhat SB. Manifestation, complications and clinical outcome in paraquat poison: a hospital based study in a rural area of Karnataka. J Environ Occup Sci. 2014;3(1):21–24.
16. Prasad DRMM, Chennabasappa A. Outcome of paraquat Poisoned patients Treated with a commonly used therapeutic flowchart: a case series. Asia Pac J Med Toxicol. 2015;4:139–142.
17. Kanchan T, Bakkannavar SM, Acharya PR. Paraquat poisoning: Analysis of an uncommon cause of fatal foisoning from Manipal, South India. Toxicol Int. 2015;22(1):30–34.
18. Weng CH, Chen HH, Hu CC, Huang WH, Hsu CW, Fu JF, Lin WR, Wang IK, Yen TH. Predictors of acute kidney injury after paraquat intoxication. Oncotarget. 2017 May 18;8(31):51345-51354. doi: 10.18632/oncotarget.17975. PMID: 28881652; PMCID: PMC5584253.
19. Wang WJ, Zhang LW, Feng SY, Gao J, Li Y. Sequential organ failure assessment in predicting mortality after paraquat poisoning: A meta-analysis. PLoS One. 2018 Nov 16;13(11):e0207725.