ORIGINAL RESEARCH PAPER

Volume-8 | Issue-3 | March-2019 | PRINT ISSN No 2277 - 8179

INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

CLINICAL PROFILE AND OUTCOMES OF PATIENTS ADMITTED FOR PARAQUAT POISONING IN A TERTIARY CARE HOSPITAL.

Medicine

Manoj Kumar Ch — Professor, Department of General Medicine, Dr. Pinnamaneni Siddhartha Institute of Medical Sciences and Research Foundation, Chinoutpalli, Krishna Dist, Andhra Pradesh, India.

Kamalakar Penubothu* — Post Graduate Student, Department of General Medicine, Dr. Pinnamaneni Siddhartha Institute of Medical Sciences and Research Foundation, Chinoutpalli, Krishna Dist, Andhra Pradesh, India. *Corresponding Author

Priyanka Jangam — Post Graduate Student, Department of General Medicine, Dr. Pinnamaneni Siddhartha Institute of Medical Sciences and Research Foundation, Chinoutpalli, Krishna Dist, Andhra Pradesh, India.

ABSTRACT

Background and objective: As India being farming based country we often tend to see patients present to emergency department following Paraquat ingestion with intention of self harm. There is relatively less awareness about Paraquat poisoning in comparison to Organophosphate compound poisoning.

Aims & Objectives: To find a clinical feature that can predict outcome, and specific intervention that can improve outcome in Paraquat (PQ) poisoning cases.

Methods: 30 patients with history of Paraquat consumption admitted at Dr PSIMS & RF, hospital during the time period December 2016 to December 2018.

Results: Of the 30 patients 21 were male and 9 females. 2 of the patients survived following poisoning while 28 expired. Paraquat dichloride 20% was the compound consumed commonly. High anion gap metabolic acidosis (HAGMA) was seen in all the patients. 12 (40%) patients underwent hemodialysis and 10 (33.3%) were mechanically ventilated.

Conclusion: Study showed high mortality in Paraquat poisoning.

KEYWORDS

Paraquat Poisoning, High Anion Gap Metabolic Acidosis, Hemodialysis, Mechanical Ventilation.

Introduction:

Paraquat (1, 1-dimethyl-4, 4-bipyridinium) is a widely used nonselective contact herbicide. That is primarily used in agriculture for control of weeds. In the Indian market it is available as liquid concentrate as 29.1% for agricultural use[1]. Due to lack of restriction; it is easily procurable and hence it is not rare to see patients present to emergency department following Paraquat ingestion with intention of self harm.

Mechanism through which paraquat exerts its toxic action is by generation of reactive oxygen species[2]. Paraquat is metabolized by several enzyme systems (NADPH-cytochrome P450 reductase, xanthine oxidase, NADH-ubiquinone oxidoreductase and nitric oxide synthase)[3]. Its metabolism through these systems generates a paraquat mono-cation radical (PQ. +). Inside the cell, PQ. + rapidly gets re-oxidized to PQ2+ and in the process it generates superoxide (O2 .-). O2 acts as an electron acceptor and NADP as an electron donor in this reaction. This further gives rise to formation of the hydroxyl free radical (HO). Further more in the presence of iron via the Fenton reaction; NO combines with O2 to generate peroxinitrite (ONOO-) this is a very strong oxidant and a nitrating intermediate. NO is enzymatically produced from L-arginine by NO synthase and PQ also directly or indirectly induces NO synthase mediated nitric oxide production[4]. Generation of highly reactive oxygen and nitrite species results in toxicity in most organs but the toxicity is particularly severe in the lungs as paraquat is taken up against a concentration gradient in to the lung.

The bioavailability of paraquat in humans is estimated to be less than 5%, yet an oral exposure of as little as 10 mL allows sufficient paraquat to be absorbed for significant clinical toxicity to occur. Absorption is rapid and the peak concentration occurs within 1 hour. Co-ingestion of food may decrease the absorption of paraquat. Recently, paraquat was reformulated with an increased emetic concentration along with an alginate that formed a gelatinous mixture on contact with gastric acid, limiting release of the paraquat into the stomach[5]. Paraquat is available as 5%/10%/15%/20% concentration forms.

Paraquat binds minimally to serum proteins. In humans the distribution half-life is approximately 5 hours. Paraquat accumulates in alveolar cells so the concentration exceeds that of the blood, with a peak occurring at around 6 hours post-ingestion in patients with normal renal function and a delay being recognized with renal impairment. However, this accumulation appears to be a reversible process given that paraquat redistributes back to the systemic circulation as its concentration falls. This is possibly due to impaired function of the pneumocytes from acute lung injury. The uptake of paraquat is an energy- dependent process that continues as long as the blood concentration of paraquat remains elevated. Paraquat is not metabolized and elimination is primarily renal with more than 90% of a dose being excreted within the first 24 hours of poisoning if renal function is maintained[6]. Its clearance initially exceeds that of creatinine mostly because of active secretion. Renal clearance may be reduced by exogenous compounds or an acidic urine pH.

Routes of exposure: through skin, eye contact, inhalation, ingestion.

Effect on organ systems:

Lungs: Paraquat toxicity is most severe in the lungs and leads to an acute alveolitis. Paraquat concentrates in alveolar type I and II cells *via* an energy dependant transport system. Further effects include diffuse alveolar collapse, vascular congestion and adherence of activated platelets and polymorphonuclear leucocytes to the vascular endothelium. In the lung, as in most tissues, paraquat toxicity leads to apoptosis of affected cells. During the acute 'destructive phase' both type I and type II pneumocytes demonstrate swelling, vacuolation and disruption of mitochondria and the endoplasmic reticulum[11]. Sloughing of the alveoli is associated with pulmonary oedema. This initial phase is followed by a proliferative phase where the alveolar space is filled with mononuclear profibroblasts which mature into fibroblasts within days to weeks. This stage is followed by lung fibrosis[5].

Kidney: Paraquat is actively secreted by the kidney via organic cation transport systems. Kidneys exposed to paraquat demonstrate development of large vacuolation in proximal convoluted tubules which leads to necrosis. It is an early, but often reversible, feature of paraquat poisoning. Maintenance of renal function reduces plasma paraquat levels and thereby minimize accumulation in lung cells[6].

Liver: Congestion and hepatocellular injury associated with rough and smooth endoplasmic reticulum degranulation and mitochondrial damage occur in the liver. These changes can be observed within a few hours to days[6].

AIMS & OBJECTIVES:

In this study we present clinical features, treatment details and prognosis of 30 cases who were admitted at our institute with Paraquat poisoning. Our objective is to find out if there is any clinical feature and any intervention that can predict the outcome. The interventions were based on the available clinical data.

MATERIALS & METHODS:

It is a prospective study carried out at Dr. PSIMS & RF during December 2016- December 2018. 30 patients admitted to this hospital with paraquat poisoning were enrolled into the study. Among them 21 were males, 9 females.

Inclusion criteria: all the patients admitted with Paraquat ingestion were included in the study.

Variables and measurements: Haemogram, urine analysis, arterial blood gas analysis, serum electrolytes, renal and liver function tests and chest radiography.

RESULTS:

Table 1 : Gender and Age based distribution

	Male	Female	Dead	Alive
10-20	1	1	2	-
21-30	8	4	12	-
31-40	6	2	8	1
41-50	5	1	6	-
51-60	1	1	2	1
total	21	9	28	2

Of the 30 patients 21 were male and 9 female. Of them 28 expired and 2 survived. Of the two survived patients one was female in age group 31 to 40 and other was male in the age group 51 to 60 years. Mean age of the subjects in the study is 33 years.

Table 2 : Quantity of PQ

PQ quantity	Frequency	Death	%
<5ml	4	2	50%
6-10ml	4	4	100%
11-15ml	2	2	100%
>15ml	20	20	100%
total	30	28	

It is observed in this study that 50% of the patients who consumed <5 ml of PQ have survived and 50% expired which showed PQ is highly toxic even in minimal quantity.

Table 3: Complications

Time	Complications			
	HAGMA	AKI	ARDS	Hepatitis
<2hrs	4	-	-	-
2–12 hrs	7	1	-	-
12–24 hrs	5	3	1	1
24–48 hrs	6	6	3	4
3–5 days	3	3	2	2
5–7 days	3	3	3	2
>7days	2	2	2	1

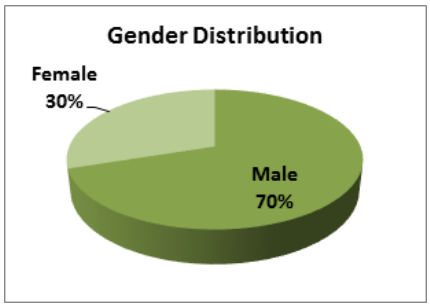
Above table showed that 100% of the subjects in the study presented with HAGMA. Eventually they progressed to have multiple organ dysfunction. Mortality was 93.3% in the study subjects.

Table 4: Interventions

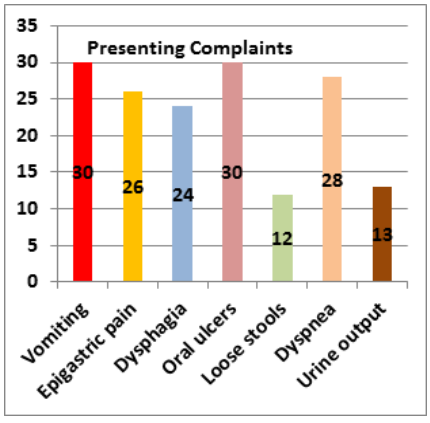
Variable	Number of Patients	Percentage
Mechanical Ventilator	10	33.3%
Hemodialysis	12	40%
Gastric lavage	30	100%
Activated Charcoal	30	100%
N- Acetylcysteine	25	83.3%
Steroid	10	33.3%

Above table showed the interventions tried in the patients. In spite of interventions mortality is high.

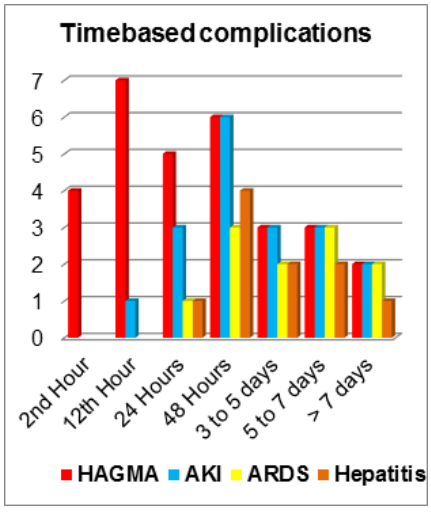
Graph 1: shows 70% of Paraquat poisoning cases case are males and 30% are females.



Graph 2: shows the proportion of patients with their presenting complaints



Graph 3 : shows the time based complications in the study group. As per our observation among 4 subjects presenting at second hour all 4 of them had HAGMA. And further observed subjects at below mentioned time period developed AKI ,ARDS, hepatitis subsequently



Graph 4: Percentage of complications encountered in the study group

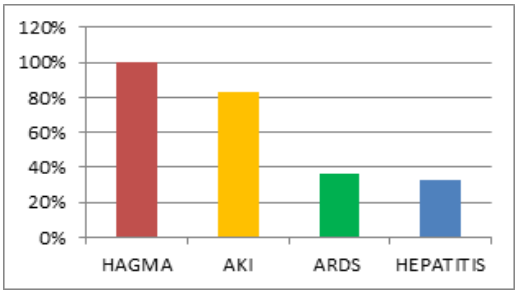


Table 5: Prognosis

Prognosis	Number of Patients
Recovery	2 (6.6%)
Mortality Within 24hrs of admission Time to death after ingestion	28(93.3%) 3 4.5 days

Above table is about the percentage of mortality in the study. There were 3 deaths within 24 hours of duration from intake. Mean duration of death in the sample is 4.5 days.

DISCUSSION:

30 patients admitted with paraquat poisoning were enrolled in the study. Among them 21 were males, 9 were females. Most of them belonged to the age group of 21- 30 years. Almost everyone suffered vomiting episodes, epigastric pain and oral ulcers with quick progression to having dysphagia and odynophagia.

Gastric lavage and activated charcoal were given to all patients at ER. N-acetyl cysteine (NAC) and vitamin c was given to 25 patients[7]. 12 patients underwent dialysis and 10 patients required mechanically ventilated secondary to respiratory failure. However the intervention didn't prevent mortality.

In the present study majority (66.6%) of patients presenting with Paraquat consumption had taken 20 % Paraquat. Only 4 patients (13.3%) have taken 5% Paraquat. Those who have taken less quantity of 5% paraquat survived for longer period in comparison to the patients with large amount of paraquat intake. However the prognosis was bad in both groups. Only two people who survived in this study had taken 5 ml of 5% Paraquat. Complications had set in almost all cases including the survivors suggesting even low dose can cause symptoms and end organ damage but may not be fatal[8].

CONCLUSION:

It is observed that the earliest sign of systemic involvement is metabolic acidosis with High Anion gap. It was evident within two hours with no or little change in PO2 and SpO2. Though there are lab tests proposed in the evaluation of the paraquat poisoning; the tests are not easily available. A thorough history and ABG remain the most important tools followed by renal and liver function tests. Paraquat poisoning has high mortality rate, either patient had acute kidney injury or respiratory failure or both.

In our study HAGMA is the early laboratory change noted in almost all patients occurring as early as second hour post consumption. ABG done at presentation to ER may help to access the severity and further guide need for early RRT. Early hemodialysis for prevention of AKI needs to be studied further.

REFERENCES:

1. Narendra SS, Vinaykumar S. Paraquat Poisoning: A Case Series in South India. International Journal of Science and Research (IJSR). 2013:2319-7064.
2. Gawarammana IB, Buckley NA. Medical management of paraquat ingestion. British journal of clinical pharmacology. 2011 Nov 1;72(5):745-57.
3. Peng J, Stevenson FF, Oo ML, Andersen JK. Iron-enhanced paraquat-mediated dopaminergic cell death due to increased oxidative stress as a consequence of microglial activation. Free Radical Biology and Medicine. 2009 Jan 15;46(2):312-20.
4. Ahmad I, Kumar A, Shukla S, Prasad Pandey H, Singh C. The involvement of nitric oxide in maneb-and paraquat-induced oxidative stress in rat polymorphonuclear leukocytes. Free radical research. 2008 Jan 1;42(10):849-62.
5. Dinis-Oliveira RJ, Duarte JA, Sanchez-Navarro A, Remiao F, Bastos ML, Carvalho F. Paraquat poisonings: mechanisms of lung toxicity, clinical features, and treatment. Critical reviews in toxicology. 2008 Jan 1;38(1):13-71.
6. Silva R, Vilas-Boas V, Carmo H, Dinis-Oliveira RJ, Carvalho F, de Lourdes Bastos M, Remião F. Modulation of P-glycoprotein efflux pump: induction and activation as a therapeutic strategy. Pharmacology & therapeutics. 2015 May 1;149:1-23.
7. McCarthy S, Somayajulu M, Sikorska M, Borowy-Borowski H, Pandey S. Paraquat induces oxidative stress and neuronal cell death; neuroprotection by water-soluble Coenzyme Q10. Toxicology and applied pharmacology. 2004 Nov 15;201(1):21-31.
8. Gil HW, Kang MS, Yang JO, Lee EY, Hong SY. Association between plasma paraquat level and outcome of paraquat poisoning in 375 paraquat poisoning patients. Clinical toxicology. 2008 Jan 1;46(6):515-8.