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A REVIEW ON INCIDENCE, CLINICAL FEATURES AND MORTALITY IN PARAQUAT POISONING PATIENTS

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ABSTRACT

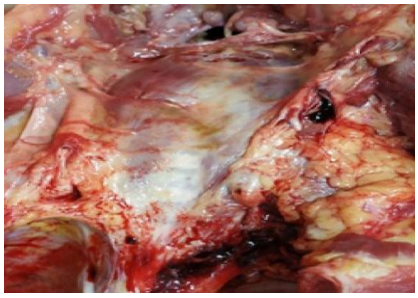
A xenobiotic that is poisonous to the body is called a poison. Depending on the exposure, poisoning may happen on purpose or by accident. When exposed to the poison for an extended period, illness may take several days, weeks, months, or even years to manifest. Because of its effectiveness and minimal environmental toxicity, paraquat is well known. No matter how much paraquat is consumed, the consequences on the GIT, kidney, liver, lungs, and other organs can be fatal. The fatality/death/mortality rate from intentional/ accidental exposure to paraquat increases in the absence of a particular antidote. Thus, we analyzed the literature with an emphasis on paraquat poisoning publications to shed light on its prevalence, clinical manifestations, and death through renal, respiratory, and multi-organ failure/damage.

KEYWORDS: Mortality, Antidote, Multi-organ failure, Renal failure, Respiratory failure, and GIT (Gastrointestinal tract).

INTRODUCTION

Paraquat (1,1[1]-dimethyl1-4,4[1]-bipyridylium dichloride) is used as a Broad-Spectrum herbicide with low price discovered in 1955 in many developing countries, suicide with the

use of pesticide is a major problem with approximately 3 lakh deaths in Asia-pacific region.[1,2,3] The clinical manifestation of paraquat poisoning is due to the production of intracellular reactive oxygen species, which causes cell damage through activation of nuclear factor kappa B, mitochondrial damage, lipid peroxidation, and apoptosis in many organs. Through the same mechanism, paraquat causes damage to the lungs, myocardium, kidneys, adrenal glands, liver, and central nervous system (CNS) which sometimes leads to multi-organ failure.[4] Intentional Poisoning due to paraquat is an important cause of mortality, especially due to the lack of a specific antidote.[2] Despite the variety of treatments proposed for paraquat poisoning, there exists a 50-90% mortality rate which is too high.[4] Paraquat is a pungent corrosive liquid and marked commonly as 'All Quit', 'Finish', 'Gramex', 'Gramo', 'Gramoxone' etc, in India, and the ingestion of paraquat irrespective of quantity may be fatal with life-threatening effects of GI tract (Gastrointestinal tract), kidney, liver, lungs, and other organs leading to multi-organ damage and thereby leading to morbidity and mortality.[5] Paraquat consumption >40 mg/kg causes rapid multi-organ failure and death (within the first 2 days), but consumption of 20 mg/kg only results in minor symptoms, and most people survive.[2] The majority of victims, even those who have only taken a small amount, will die from paraquat poisoning because it is such a deadly condition.[1] Pulmonary fibrosis is the leading cause of death in most cases.[1] According to estimates from the World Health Organization, between 2004 and 2012, unintentional poisoning is thought to have killed between 193,000 and 346,000 individuals globally.[6,7] 84–91% of these fatalities took place in low- and middle-income nations (LMICs). Unintentional poisoning resulted in a loss of over 7.4 to 10.7 million years of healthy life (life years adjusted for handicap) between 2004 and 2012.[6,7] Although there were fewer fatalities between the two reports, there was an increase in the number of years with a disability-adjusted life expectancy (2004 vs. 2012).[6] Suicide is the leading cause of death for people worldwide between the ages of 15 and 29.[6] In addition, 79% of suicides in 2016 took place in LMICs.[6]



Yellowish discoloration and erosions on the inner wall of the trachea[5]

Paraquat tongue (Ulceration on dorsum of tongue with discoloration)[5]

DISCUSSION

Study - 01: Gheshlaghi *et al*., (2022) conducted a study on the prediction of mortality and morbidity following paraquat poisoning based on the trend of liver and kidney injury in which 24 patients were excluded because of a negative dithionite test within 24 hours. Forty-one (64.06%) patients met the study criteria. The mean (SD) age of the patients was found to be 28(±8.6) years. Most of the patients were male (n=36, 87.8%). The mean (SD) Creatinine (Cr), ALT, and AST at the time of admission were as follow1.0 (±0.4) µg/dl; 20.4(±14.4) IU/L and24.7 (±18.1) IU/L; respectively. Eighteen patients (44%) died and all of them were found to be male. A rise in creatinine was strongly linked to the mortality risk brought on by paraquat consumption. In addition, individuals who passed away had slight increases in ALT and AST. Although all of the presentations were linked to paraquat use and no other causes of liver injury were identified in our investigation, our current research may not definitively link liver injury to mortality.

Study 02: R Ravichandran *et al*., (2020) conducted a study on paraquat poisoning in which 55 patients in all were included. The majority of these patients (65.4%) were men, and the median age was 28. 32.7% of patients experienced hypotension, 61.8% had lung damage, and 10 of the 35 patients who had chest X-rays had infiltrated. Two patients had computed tomography chest, which was found to be normal, and six individuals had paraquat tongue. 81.8% of patients had acute kidney injury (AKI), and 56.3% had received dialysis. The death rate was found to be 72.7%, and all of the patients passed away within three days of consuming paraquat. During hospitalization, 35 perished and 5 were released against the medical recommendation. Acute renal injury and lung injury were revealed to be the most frequent causes of these deaths.

Study 03: Manas Ranjan Sahu *et al*., (2020) 12 patients with a history of paraquat ingestion were admitted during the study period for a study on the clinical and pathological profile of paraquat poisoning cases. The highest and lowest ages recorded were 42 and 18, respectively, and both of the individuals were men. The majority of sex was discovered to be males. The ages of the 5 cases ranged from 20 to 37 years for females. Early signs and symptoms in all instances included throat pain, trouble swallowing, and hoarseness of voice, vomiting, reduced urine, and loose stools. After consuming paraquat poison for 72 hours, one of the instances showed up at a nearby hospital with additional symptoms like icterus and shortness of breath (SOB). There were 5 occurrences when "paraquat tongue" was seen. Damage to the

respiratory system was shown to be the primary factor in mortality, followed by damage to the GIT (gastrointestinal tract) and kidneys. Thus, the primary causes of mortality were multi-organ failure and respiratory failure. Out of 12 cases, 11 people died, and one was released after only two days in the hospital. Despite advances in treatment and supportive care, mortality rates have been found to be increasing by up to 90%. Inheriting toxicity and a lack of definitive treatment are to blame for a high rate of paraquat fatalities.

Study 04: Zohreh Oghabian *et al.*, (2019) undertook a study to examine the clinical characteristics and mortality of paraquat poisoning. Only 126 of the 198 patients were included in the study. 50.8% (64) of the 126 individuals exposed to paraquat were married, 1.2% (2) had a history of past suicidal attempts, and 4.2% (3) had mental illnesses. Males made up 50% (63) of the group. 48.4% (61) had intentionally poisoned themselves, while 48.4% (61) had unintentionally ingested poison. 81 (63.6%) of the 126 patients in this group survived. Based on observed results, the frequency distribution of various symptoms showed that the greatest number of fatalities occurred in patients exhibiting respiratory distress (n=41), followed by oral ulceration (n=38), and excessive salivation (n=37). The lowest/fewest number of deaths occurred in patients with duodenal involvement (n=0), next in those with gastric involvement (n=1). Therefore, paraquat poisoning is associated with mortality.

Study 05: Halesha B.R *et al.*, (2018) conducted a study in which out of 110 patients 66%(n=72) were females and 44 %(n=38) were males in which most of the patients were between the age group of 30-40 years. 21%(n=24) patients survived. The most common symptoms in these patients were found to be nausea followed by cough and throat pain and the most common signs in these patients were found to be oral cavity ulcers followed by tachypnea and tachycardia. The most common organ complication was found to be acute renal failure 77% (n=85), followed by hepatic dysfunction 59%(n=65), respiratory failure 49%(n=54), and multi-organ dysfunction 46%(n=50) patients. The overall mortality was presented in 80 patients (72%), 20(18%) patients recovered fully and 10 patients (10%) left against medical advice.

Study 06: Narcisse Elena *et al.*, (2017) conducted a study on the clinical characteristics and prognosis of paraquat poisoning, finding that the yearly incidence was 3.8/100,000 people/years. There were 62 individuals involved (30 males and 32 females). There were 62 patients, including 44 adults and 18 kids under the age of 16. The median ages for adults

were 31 years (18.08–75.25) and for children, they were 13.4 years (0.75–15.08). Clinical and biological signs at presentation included vomiting before hospital admission in all included patients, with epigastric discomfort and oral mucosal irritation in 22 patients (32%), and paraquat being discovered concurrently in the urine and gastric fluid in 13 patients. Oesogastroduodenal microscopy revealed lesions in all of these patients. Liver cytolysis was present in 55% of the individuals. 50% of adult patients with a creatinine level of greater than 120 mol/L upon admission died, and only 2 individuals did not experience a second episode of creatininemia despite having a very high initial creatinine level. Eighty-two percent of patients with a Yamaguchi score I<930-399 log T died, while ninety-two percent of those with a Yamaguchi score I>1500-399 Log T survived. The amount of paraquat consumed was discovered to be the main factor linked to death.

Study 07: Jagadeesan M *et al*., (2017) conducted a study in which a total of 10 patients with paraquat poisoning were included in the study. All 10 cases were suicidal cases who had ingested liquid paraquat concentrate. The median age of the patients was found to be 28.5 years and 80% of the paraquat-poisoned patients was found to be male. 40% of the patients (n=4) died due to multi-organ dysfunction syndrome and 20% of patients (n=2) died due to ARDS (acute respiratory distress syndrome). Therefore, multi-organ dysfunction/failure was found to be the main common cause of death in patients with paraquat poisoning. 8 patients (80%) developed acute kidney injury (AKI) with metabolic acidosis and among these 8 patients, 5 of them had severe metabolic acidosis and one of the patients also developed pneumomediastinum after ingestion of paraquat. As a result, administrative steps must be taken to limit the availability of this lethal herbicide on the market.

Study 08: Mohammad Delirrad *et al*., (2015) conducted a study in which the prevalence and clinical characteristics of paraquat poisoning were examined. A total of 41 cases were examined. Males made up the majority (56.1%, n=23). The ratio of men to women was 1.28. The mean standard deviation (SD) of the patient's age and length of hospitalization were respectively 5.754.6 days and 31.616.9 years. It was discovered that the in-hospital death rate was 46.4 %(n=19), with 33.3 %(n=6) for females and 56.5 %(n=13) for males. All patients who consumed more than 150ml (n=12) decreased, compared to patients who consumed less than 25ml (n=14). The survival rate for patients who consumed 30-150 ml was 50% (n=10). The majority of the patients in the study had epigastric discomfort (36.6%), vomiting (43.9%), nausea (53.7%), mucosal lesions of the oral cavity and pharynx (85.4%), fever (9.8%), and

loss of consciousness in the form of mild to moderate fatigue (9.8%). Respiratory failure (31.6%, n=6), multi-organ failure (57.9%, n=11), hemorrhage (2.4%, n=1), and cardiogenic shock (2.4%, n=1) were the most frequent causes of death.

Study 09: Fazel Goudari *et al.*, (2014) conducted a study in which mortality analysis of patients with paraquat poisoning was studied and 6584 patients with different types of poisoning were hospitalized among them 52 patients were poisoned with paraquat (0.8%). Out of 52 paraquat-poisoned patients, 73.1% were men. The average age of paraquat-poisoned patients was found to be 28.2 ±10.3 years, with a range of 15 to 60 years. The most common clinical symptoms of patients were nausea and vomiting (88.5%), epigastric pain (80.8%), and pharyngeal congestion (82.7%). Of the patients, 27 (51%) died, 24 (24%) were able to be discharged without any further complications, and one (1) was discharged with minor gastric irritation.

Study 10: Harshavardhan L *et al.*, (2014) conducted a study in which 77 patients were presented with acute paraquat poisoning and it was 2.2 times more among males. Acute renal failure was found to be 45.5%, hepatic involvement 35%, acute respiratory failure 16%, circulatory failure 11%, GIT lesions 48%, and multi-organ failure 22%. Among 77 cases only 60 cases were included in the study (n=60), 21 poisoning-related fatalities were reported, and was found that predominantly male patients were involved (61%). Moreover, most of the patients who did not survive had ingested > 40ml of paraquat (76.19%). And the cause of mortality was found to be acute renal failure (76.19%), followed by multi-organ failure (66.66%), respiratory failure (42.85%), shock (23.8%), and hepatic involvement (14.28%). Patients who have taken less than 20ml recover faster.

CONCLUSION

Paraquat is one of the most common and widely used weedicides globally and in most countries. It is been used without any restrictions however, it was restricted to be used in some countries. This review concludes that suicidal ingestion was the most incident and more predominant in males according to the above studies which were taken into consideration. Patients who ingested >40 -50 ml of paraquat were dead, all of them which were intentional, and some patients who consumed <20 ml were found to be having better recovery. Paraquat poisoning is associated with high mortality requiring an immediate assessment of patients because of the onset of action related to the amount consumed, which is directly proportional to the increased risk of death. The most common presenting symptoms were difficulty in

swallowing, nausea, vomiting, and mouth ulcers, and the causes of death were attributed to GI, respiratory, kidney, liver, and multi-organ damage or failure.

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Conflict of interest

The authors confirm that this article's content has no conflicts of interest.

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