

## Demographics, Clinical Characteristics and Management of Herbicide Poisoning in Tertiary Care Hospital

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### ABSTRACT

Herbicide poisoning is most common method of suicide in India and it is associated with high morbidity and mortality. Among different herbicidal poisonings the most predominantly found poisonings are paraquat and glyphosate. These compounds are highly toxic and their poisonings require proper management techniques. High fatality is seen in these cases which are mainly due to its inherent toxicity and lack of effective treatment. Common symptoms of these poisonings includes gastrointestinal corrosive effects with mouth and throat, epigastric pain and dysphagia, acid-base imbalance, pulmonary edema, shock and arrhythmia. Long term health effects include pulmonary fibrosis, renal failure, hepatic failure, heart failure, multi-organ failure or death. No proven antidote exists for these poisonings. So the treatment is mainly supportive. Initially gastric lavage or whole-gut irrigation using adsorbents such as Fuller's earth, bentonite or activated charcoal is recommended. In case of renal failure hemodialysis or hemoperfusion may be considered. However novel approaches like treatment with N-acetylcysteine, vitamin C, vitamin E, cyclophosphamide may also be helpful.

**Key words:** Glyphosate, herbicide, poisoning, paraquat, treatment

### INTRODUCTION

Poisoning from pesticides and other agricultural chemicals is a major public health problem worldwide, especially in the developing countries. Among them, herbicides like paraquat and glyphosate are most common poisonings responsible for high morbidity and mortality. Paraquat (1, 1'-dimethyl-4, 4'-bipyridium dichloride) is non-selective contact herbicide that is relatively widely-used. It is a very dangerous pollutant of the environment, as it readily binds

to both clay and organic matter in soil and is very slowly biodegraded.<sup>[1]</sup> This acute poisoning is common method of suicide in India.<sup>[2]</sup> Poisoning due to this chemical is observed because of the easy availability, improper storage methods and lack of awareness of the potential harm. As they are highly toxic compounds, management of these poisonings requires a great deal of skill and knowledge of proper management procedures.<sup>[3]</sup> Toxic effects of paraquat originate from the production of free radicals formed by the cyclic oxidation-reduction reactions of the compound in tissues.<sup>[4]</sup> The symptoms after ingestion are burning sensation in the mouth, throat, chest, upper abdomen, nausea, vomiting, abdominal pain and diarrhea. These gastrointestinal symptoms settle after 2-3 days if the patient survives. Ulceration of the mouth, acute renal failure and jaundice may follow a few days later. The early or delayed appearance of respiratory distress or failure is one of the characteristic feature of the condition.<sup>[5]</sup> Common symptoms of central nervous system (CNS) and

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other systems include giddiness, headache, fever, myalgia, lethargy and coma. High fatality is seen in these cases which are mainly due to its inherent toxicity and lack of effective treatment. For treatment of these poisoning there are no widely accepted guidelines.<sup>[6]</sup> To prevent systemic toxicity due to intoxication of these chemicals immediate treatment is necessary. In case of ingestion of herbicides like paraquat and glyphosate gastric lavage or whole-gut irrigation using adsorbents such as Fuller's earth, bentonite or activated charcoal is recommended.<sup>[7]</sup>

Glyphosate is a non-selective herbicide. The mechanism by which glyphosate causes toxicity is complicated due to its composition. Common symptoms of this poisoning include gastrointestinal corrosive effects with mouth and throat, epigastric pain and dysphagia. In severe cases, impaired consciousness, arrhythmias, pulmonary edema, shock, renal failure requiring hemodialysis, hyperkalemia and metabolic acidosis are also seen. There is a sensible relationship between the amount of compound ingested and the effects caused by it.<sup>[8]</sup> There is no specific antidote for glyphosate and treatment is mainly supportive or activated charcoal and gastric lavage can be considered in patients who are admitted within one hour after ingestion of poison.<sup>[9]</sup>

## Objectives

In the present study we aimed to study the demographics of patient, clinical characteristics and treatment pattern for herbicide poisoning in tertiary care hospital.

## MATERIALS AND METHODS

A retrospective observational study was conducted on patients with herbicide poisoning admitted in emergency ward of tertiary care Hospital in South India between January 2004-2012. Sixty patients were included in the study. A detailed history had been taken from the patient records of medical record section. Demographic characteristics like age, sex, type of exposure, pre-hospitalization period, clinical features, type of compound along with treatment and outcome were obtained from the patient files. These were recorded using standardized data collection forms and were analyzed using SPSS 16.0 package.

## RESULTS

During the study period, 60 patients of Herbicide poisoning were admitted to the emergency ward of tertiary care Hospital in South India. Gender wise distribution showed that majority of them were males which constitute 60% of the study population. There were 36 male and 24 female patients and the male/female ratio was almost 3:2. The median age of the study population was found to be  $25.38 \pm 9.136$  yrs. Majority of poisoning were

intentional (95%). The median pre-hospitalization period was found to be 3.50 (9.25) hrs. The clinical characteristics of herbicide poisoning patients mainly includes incidence of vomiting 41 (68.3%), oral ulcers 19 (31.7%), throat discomfort 16 (26.7%), abdominal pain 14 (23.3%), dysphagia 10 (16.7%) and dyspnea 6 (10.0%). Among the study population, 6.7% ( $n = 4$ ) of patients had psychiatric illness. Table 1 presents the basic demographic details of paraquat poisoning patients. Different herbicide compounds consumed are paraquat 47 (78.3%) and glyphosate 13 (21.7%). Herbicide compounds consumed by the patients are given in Table 2. Among the study population majority of them were students  $n = 15$  (25.0%) followed by farmers ( $n = 12$  (20.0%). Details are given in the Table 3. Among the different treatment approaches majority of the patients 22 (36.7%) received gastric lavage and 16 (26.7%) patients received activated charcoal at initial stage of therapy. Among 60, 30 (50.0%) patients received N-acetylcysteine (NAC), 23 (38.3%) patients received steroids, furosemide 16 (26.7%), vitamin C 15 (25.0%), cyclophosphamide 13 (21.7%) and Vitamin E 11 (18.3%). A total of 16 (26.7%) patients underwent hemodialysis and

**Table 1: Demographical and clinical characteristics of herbicide poisoning**

Patient's demographic characteristics	
Mean age SD in years	25.38±9.136
Male sex, n (%)	36 (60)
Poisoning exposure	
Suicidal, n (%)	57 (95.0)
Pre hospitalization period median (IQR) in hours	3.50 (9.25)
Patient clinical characteristics (n (%))	
Vomiting	41 (68.3)
Oral ulcers	19 (31.7)
Throat discomfort	16 (26.7)
Abdominal pain	14 (23.3)
Dysphagia	10 (16.7)
Dyspnea	6 (10.0)
Co-morbid illness	
Psychiatric illness, n (%)	4 (6.7)

SD = Standard deviation, IQR = Interquartile range

**Table 2: Percentage of different herbicide poisoning**

Herbicide compound	Frequency (%)
Paraquat	47 (78.3)
Glyphosate	13 (21.7)

**Table 3: Occupation and Herbicide poisoning**

Occupation	Frequency of poisoning (%)
Student	15 (25.0)
Farmer	12 (20.0)
Coolie	5 (8.3)
Business	2 (3.3)
Others	26 (43.3)

hemoperfusion was done only in 4 (6.7%). The outcome analysis of herbicide poisoning cases admitted during study period, 23 (38.3%) of them recovered, 37 (61.7%) of them were expired.

Details regarding treatment and outcome are given in Table 4.

## DISCUSSION

In the present study the Herbicide poisoning cases included were of paraquat (78.3%) and glyphosate (21.7%). Gender wise distribution of study population showed that males (60%) predominated over females (40%). The male to female ratio was 1.5:1 with mean age of  $25.38 \pm 9.136$  years. A similar study conducted in Soonchunhyang Hospital (SCH) in Cheonan, Korea by Kim *et al.*, 2009 showed similar results with male to female ratio of 1.3:1 with mean age  $26.58 \pm 9.473$  years in males and mean age of  $23.58 \pm 8.480$  years in females.<sup>[10]</sup> In the present study, mean pre-hospitalization period was found to be  $11.250 \pm 19.96$  hrs. In a study conducted by Hong *et al.*, 2000, the mean pre-hospitalization period was found to be  $15.6 \pm 30.8$  in survivors and  $1.7 \pm 2.1$  in non-survivors.<sup>[11]</sup> This indicates that the mortality rate not only depends on pre-hospitalization period but also depends on other factors like type and amount of compound consumed. In another study conducted by Kim *et al.*, 2009, the mean pre-hospitalization period was found to be  $15.93 \pm 26.03$ .<sup>[10]</sup>

Among the total pesticide exposures herbicides accounts for 29% according to British pesticide exposure survey by the UK National Poisons Information Service in 2005. Glyphosate was the fourth most common exposure, and the third most common implicated in self-harm cases.<sup>[12]</sup> Among the total acute pesticide poisonings, the majority of deaths were from intentional self-poisoning with paraquat, organophosphorus pesticides (OP) and aluminium

phosphide.<sup>[13]</sup> In pesticide poisoning the fatality rate is between 18% and 23% with highest fatality rates in case of paraquat.<sup>[14-17]</sup> In the present study majority of the herbicide poisonings were due to deliberate self-harm (95%) with high mortality rate 61.7%.

The common clinical features of herbicide poisoning as observed in our study are as follows: Vomiting (68.3%), oral ulcers (31.7%), throat discomfort (26.7%), abdominal pain (23.3%), dysphagia (16.7%) and dyspnea (10%). As per study conducted by Sandhu *et al.*, 2003 the common symptoms for paraquat poisoning were vomiting (100%) followed by oral ulceration (59%), dysphagia (53%) and dyspnea (41%).<sup>[18]</sup> For glyphosate poisoning the clinical manifestations include corrosive effects on the gastrointestinal tract, Tachy- and brady-arrhythmias, renal failure, elevated liver enzymes, hyperkalemia and metabolic acidosis.<sup>[19]</sup>

Out of 60 patients 4 (6.7%) patients had psychiatric illness. It is one of the risk factor for the intentional self-harm. According Eddleston and Phillips psychiatric illness is the one of the major risk factor for self-poisoning. By prophylactic medical management it is possible to reduce the incidences of self harm.<sup>[20]</sup> Due to its inherent toxicity and the lack of effective treatment paraquat has high mortality rate. The treatment varies from supportive care alone to various combinations of immune-modulation, antioxidant therapy, hemoperfusion and hemodialysis as there are no widely accepted guidelines.<sup>[6]</sup>

In the present study treatment pattern analysis showed that 22 (36.7%) patients were treated with gastric lavage and 16 (26.7%) patients were treated with activated charcoal at the initial stage of therapy. Inducing emesis is not recommended instead gastric lavage might be helpful when performed within 1 hour of ingestion, although it may be useful up to 24 hours after ingestion.<sup>[9,21]</sup> Hemodialysis and Hemoperfusion were performed in 16 (26.7%) and 4 (6.7%) respectively. In our study out of 60 patients 17 patients had developed acute renal failure and 8 of these patients were given dialysis for acute renal failure (Hemodialysis in six and Hemoperfusion in two). A study conducted by Koo *et al.*, supports that the accumulated paraquat elimination from lungs depends minimally on plasma concentration. An uncontrolled study conducted by Koo *et al.*, showed that number of survival days were prolonged but there was no difference in mortality when hemoperfusion is given along with continued venovenous hemofiltration (CVVH) when compared to hemoperfusion alone in a group of 80 patients with paraquat self poisoning and mortality between these two groups was found to be 63.6% versus 66.7%.<sup>[22,23]</sup>

The major event of free radical injury primarily affects the lungs therefore the use of anti-oxidants was supported by

**Table 4: Different treatment pattern in herbicide poisoning**

Type of treatment (%)	
Gastric lavage	22 (36.7)
Activated charcoal	16 (26.7)
N-acetyl cysteine	30 (50.0)
Steroids	23 (38.3)
Furosemide	16 (26.7)
Vitamin C	15 (25.0)
Vitamin E	11 (18.3)
Cyclophosphamide	13 (21.7)
Hemodialysis	16 (26.7)
Hemoperfusion	4 (6.7)
Outcome (%)	
Recovery	23 (38.3)
Fatal	37 (61.7)

some groups (Vitamin C 4000 mg/day and Vitamin E 250 mg/day) even though their efficacy is unproven.<sup>[24,25]</sup> In the present study vitamin C was given in 15 (25%) and vitamin E in 11 (18.3%). There were very few studies carried out to evaluate the role of vitamin C and vitamin E in paraquat poisoning. An observational study conducted by Yasaka *et al.*, 1986 in nine patients showed that the mortality rate was 78% in patients who received vitamin E<sup>[26]</sup> and observational study in five patients conducted by Hong *et al.*, 2002 showed that the mortality rate was 0% in patients who received vitamin C.<sup>[27]</sup>

The effectiveness of pulse therapy using steroids and cyclophosphamide in preventing pulmonary fibrosis was supported by some authors.<sup>[28,29]</sup> Assessment of therapy in our study showed that 23 (38.3%) were given steroids and 13 (21.7%) were given cyclophosphamide.

An observational study in five patients conducted by Agarwal *et al.*, 2006 showed that the mortality rate was 60% in patients who received steroids and cyclophosphamide.<sup>[30]</sup> In our study NAC was administered to 30 (50%) patients. NAC is an excellent source of sulfhydryl groups acting directly as a free radical scavenger thus having potentially beneficial effects in paraquat poisoning but it has been minimally studied in human paraquat poisoning.<sup>[31]</sup> In our study furosemide was given in 16 (26.7%) patients.

## CONCLUSION

This study showed that poisoning with herbicides is associated with high morbidity and mortality. Clinical signs and symptoms may vary widely depending upon the type and amount of compound ingested, pre-hospitalization period etc., Very limited data is available in the literature with respect to treatment pattern of herbicide poisoning. However novel approaches like treatment with NAC, vitamin C, vitamin E, cyclophosphamide, hemodialysis and hemoperfusion may be useful in reduction of high mortality rate. Controlled trials with different treatment modalities may help in giving beneficial information in these patients.

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