Original Article

A Retrospective Study on the Impact of Early Hemoperfusion on Survival Outcomes in Acute Paraquat Poisoning

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Abstract

Background: Paraquat (PQ) (1,1′-dimethyl-4,4′-bipyridinium dichloride) poisoning is a major global health issue, especially in developing countries. PQ accumulates in pneumocytes, causing cellular damage through reactive oxygen species and leading to pulmonary fibrosis. Despite medical advances, severe cases have a mortality rate exceeding 80%.

Methods: This retrospective observational study analyzed 30 patients over six months in the Emergency Medicine Department (ED) of a tertiary hospital in India. Adults (≥18 years) with confirmed paraquat poisoning, via history or positive urine dithionite test, admitted between January 2024 and June 202,4 were included after obtaining ethical committee approval. Cases were identified using ICD-10 code T60.3 and ED records. Data collected included demographics, poisoning details (e.g., time, quantity, time of presentation to ED) and clinical features like respiratory distress, altered mental status, and organ dysfunction. Patients who received early hemoperfusion (within 4 hours) of paraquat ingestion had a significantly higher survival rate compared to those who received it later.

Conclusion: The timing of HP administration appears to be associated with 30-day mortality, as indicated by the significant p-value (0.045), suggesting a potential relationship between delayed HP and higher mortality rates.

Keywords: Paraquat(PQ), Hemoperfusion (HP), Retrospective study, Acute kidney injury, Mechanical ventilation

Introduction

Paraquat (PQ) (1,1′-dimethyl-4,4′-bipyridinium dichloride) poisoning represents a significant global health challenge, particularly in developing nations where it remains widely accessible as an agricultural herbicide.[1] PQ toxicity involves the selective accumulation of PQ in pneumocytes through active transport systems, followed by redox cycling that generates reactive oxygen species, leading to cellular

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death and the progression to pulmonary fibrosis.[2] Despite advances in medical care, mortality rates in PQ poisoning consistently exceed 80% in emergency department presentations.[3]

The pharmacokinetics of PQ demonstrate a critical early phase where plasma concentrations peak within 1-3 hours post-ingestion, followed by rapid tissue distribution. Research has established that once PQ accumulates in lung tissue, the prognosis becomes extremely poor, with conventional treatments showing limited efficacy.[4] This distribution pattern suggests a narrow therapeutic window during which early intervention might prevent significant tissue accumulation. Current ED protocols typically incorporate hemoperfusion (HP) as a primary therapeutic modality, but the timing of its initiation varies significantly across centers, often delayed by several hours after presentation.[5] Currently, emergency departments face challenges including delayed recognition of PQ poisoning, variability in diagnostic confirmation methods, and logistical barriers to rapid HP initiation. Understanding the impact of early HP in this setting could lead to standardized protocols that optimize the use of this potentially life-saving intervention during the crucial early hours post-ingestion.

Methods

This retrospective observational study analyzed 30 patients for 6 months duration at the Department of Emergency Medicine, Kempegowda Institute of Medical Sciences, Bangalore, India.[6] The inclusion criteria for the study required participants to be at least 18 years old with a history of paraquat poisoning and to have been admitted over 6 months between January 2024 and June 2024. A confirmed diagnosis was necessary, either through an identifiable documented history of ingestion or a positive urine dithionite test. Institutional ethical clearance was obtained. Cases were identified through ICD-10 code T60.3 and emergency department registers.[7] Basic demographic details and specifics of poisoning such as age, gender, occupation, marital status, time of ingestion, approximate quantity consumed, and time elapsed before hospital presentation were collected. Respiratory distress, altered mental status, and signs of organ dysfunction at presentation were recorded from the hospital records.

Respiratory distress is defined as a respiratory rate of more than 22 cycles per minute (cpm) according to the Quick Sequential Organ Failure Assessment (qSOFA) criteria.[8] Altered mental status is defined as a Glasgow Coma Scale (GCS) score less than 15, according to the qSOFA criteria. Organ dysfunction is defined as an increase in the Sequential Organ Failure Assessment (SOFA) score by 2 points or more, according to the Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3).[9] Outcome variables include length of hospital stay, functional status, and all-cause mortality in 30 days. Functional status improvement of patients has been evaluated in terms of worsening renal function tests [AKI], respiratory failure, and the need for mechanical ventilation.

Results

Table 1: Comparison of demographic factors

Socio-economic status	Variables	HP within 4 hours	HP after 4 hours	p value
Age (in years)	<=20	3 (20.0)	2 (13.3)	0.201
	21 - 35	8 (53.3)	6 (40.0)	
	36 - 50	4 (26.7)	3 (20.0)	
	> 50	0 (0.0)	4 (26.7)	
Gender	Males	9 (60.0)	7 (46.7)	0.464
	Females	6 (40.0)	8 (53.3)	
Education	Up to high school	9 (60.0)	8 (53.3)	0.713
	College and above	6 (40.0)	7 (46.7)	

Table 1 shows that the analysis of socio-economic factors in relation to the timing of hemoperfusion (HP) revealed no statistically significant associations. Out of 30 patients, Mean Age is 34.30 ± 3.67 years. The gender distribution of the study was male 53% and female 47%.Younger patients (aged ≤35 years) were more likely to receive HP within 4 hours, while older individuals (>50 years) tended to receive it later because the time of presentation is earlier in the case of young adults. Gender distribution, education of the patients were comparable between the two groups (HP <4 hours vs HP>4 hours).

Table 2: Comparison of complications within 4 hours vs after 4 hrs

Complications	Variables	HP within 4 hours	HP after 4 hours	p value
Acute Kidney Injury	Present	3 (20.0)	7 (46.7)	0.047
	Absent	12 (80.0)	8 (53.3)	
Respiratory failure	Present	4 (26.7)	9 (60.0)	0.039
	Absent	11 (73.3)	6 (40.0)	
Mechanical ventilation	Present	5 (33.3)	9 (60.0)	0.143
	Absent	10 (66.7)	6 (40.0)	

The occurrence of complications has shown notable differences concerning the timing of hemoperfusion (HP), as in Table [2]. Acute kidney injury (AKI) was significantly more common among patients who received HP after 4 hours (46.7%) compared to those treated earlier (20.0%), with a p-value of 0.047. Similarly, respiratory failure was more prevalent in the delayed HP group (60.0%) than in the early HP group (26.7%), with a p-value of 0.039. Although mechanical ventilation was more frequently required in the late HP group (60.0% vs. 33.3%), this difference was not statistically significant (*p = 0.143*). Overall, complications were generally more common in patients receiving delayed HP.

Table 3: Comparison of outcomes within 4 hrs vs after 4 hrs

Outcomes	Variables	HP within 4 hours	HP after 4 hours	p value
Length of hospital stay	<30 days	8 (53.3)	11 (73.3)	0.256
	>30 days	7 (46.7)	4 (26.7)	
Functional status	Improved	5 (33.3)	2 (13.3)	0.224
	Same	3 (20.0)	1 (6.7)	
	Worse	7 (46.7)	12 (80.0)	
30-day mortality	Present	7 (46.7)	12 (80.0)	0.045
	Absent	8 (53.3)	3 (20.0)	

Among patients who received hemoperfusion within 4 hours, 8 (53.3%) had hospital stays of less than 30 days, compared to 11 (73.3%) in the delayed HP group. Conversely, prolonged hospital stays (>30 days) were observed in 7 (46.7%) of early HP patients and 4 (26.7%) of delayed HP patients. This difference was not statistically significant (*p* = 0.256), as shown in Table [3].

However, this difference was not statistically significant (*p = 0.256*). Functional status also varied by timing, with improved outcomes seen more often in the early HP group (33.3%) compared to the delayed group (13.3%). Conversely, patients with worsened functional status were predominantly in the delayed HP group (80.0%), though these findings were not statistically significant (*p = 0.224*). The timing of hemoperfusion was significantly associated with 30-day mortality. Among patients who received delayed hemoperfusion, 12 (80%) died within 30 days, compared to 7 (46%) among those who received early hemoperfusion (*p* = 0.045). Functional status at 30 days showed a trend favouring early hemoperfusion (*p* = 0.224). Among patients who received hemoperfusion within 4 hours, 3 (20.0%) had unchanged status and 7 (46.7%) worsened, while 2 (13.3%) of those who received delayed hemoperfusion improved, 1 (6.7%) remained unchanged, and 12 (80.0%) worsened.

Discussion

The initial hours following PQ ingestion represent a critical window where appropriate intervention could significantly alter patient outcomes.

In contrast to the observations from previous studies that suicidal ideation and attempts are more common among older age groups compared to younger adults, our study has shown that most patients affected by paraquat poisoning are in younger age group.[10] The reason for the same might be the availability of knowledge about the poison in younger adults compared to the older age groups.

Experimental evidence has demonstrated that HP initiated within 4 hours of PQ exposure significantly reduces mortality rates. All-cause mortality in 30 days in patients with HP initiated within 4 hours is significantly lower when compared to HP later than 4 hours (46% vs 80%, with a p-value of 0.045). Ying-Tse Yeh et al reported mean days of mortality as 4.2 days HP group and overall mortality of 80%, similar to the findings of our study. The survival time of the early HP group was not significantly higher than the late HP group.[11] Mortality depends on the time of presentation, early intervention and the amount of herbicide ingestion.

Functional status, assessed in terms of clinical and laboratory outcomes, also trended towards better outcomes in the early HP group. A larger proportion of patients treated early showed functional improvement compared to those treated later with HP (33.3% vs 13.3%) and fewer had deteriorated outcomes (46.7% vs 80.0%). [11] These trends suggest clinical relevance and underscore the importance of early intervention, even if not definitively proven within this cohort. [11] In studies done with larger sample sizes it has been proven that the liver function tests, renal function tests and blood gas indices showed significant improvement with early HP.[12,13]

A greater percentage of patients in the late HP group had hospital stays of fewer than 30 days.

However, this likely reflects early mortality rather than faster recovery, highlighting the importance of interpreting length of stay within the context of survival outcomes.

The major barrier to the implementation of early HP is logistical. In real-world emergency settings, delayed diagnosis, lack of rapid confirmatory tests and limited availability of HP equipment and trained personnel contribute to treatment delays in low and middle income countries. Therefore, standarzing protocols for the early recognition of parquat poisoning and immediate initiation of HP could significantly improve survival outcomes.[14] Point of care tests like urine dithionite test can aid in rapid diagnosis.

The pathophysiological basis for early HP intervention is supported by evidence demonstrating that PQ accumulation in lung tissue occurs through an active transport mechanism that becomes increasingly difficult to reverse once established.[15] These findings align with PQ's toxicokinetic profile, suggesting that early removal from circulation might prevent critical tissue accumulation thresholds. [16] However, the translation of these findings into emergency department practice faces challenges, including the optimal timing for HP initiation and the practical barriers to implementing early HP in clinical settings. This understanding has important implications for emergency response protocols and resource allocation in toxicology units. In the emergency department setting, the establishment of clear protocols for early HP is particularly crucial, as it represents the first point of medical contact for most poisoning cases.

Strengths:

This study addresses a highly lethal and under-researched form of poisoning and contributes valuable insights into optimising emergency treatment protocols, specifically the timing of hemoperfusion.

Limitations:

The study was conducted in a single institution, which may limit the generalisability of results to other settings, especially those with different resource availability or treatment protocols.

Conclusion:

In patients with paraquat poisoning, treatment with early hemoperfusion significantly improved 30-day survival rates. There is a reduced incidence

of kidney and respiratory failure among patients receiving early hemoperfusion therapy. This study reinforces the critical role of early hemoperfusion in improving survival and reducing complications in acute paraquat poisoning. While early HP significantly lowers mortality, its full impact depends on timely diagnosis, quick access to specialised care, and supportive treatment protocols. Larger multicentric studies and prospective designs would be beneficial to confirm these results and guide standardised emergency response strategies for PQ poisoning.

Conflict of Interest: No conflict of interest has been reported by any of the authors of this study

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