ORIGINAL ARTICLE

Factors associated with refusing hemoperfusion in patients with acute paraquat poisoning

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Background: Paraquat poisoning remains a critical public health issue with no established effective treatment. Hemoperfusion (HP) has been recognized for its potential to remove toxins and is widely employed in several developing countries for managing acute paraquat poisoning cases. However, the reluctance of some patients to undergo this recommended treatment has been observed but not thoroughly investigated. This study aimed to explore the factors associated with the refusal of HP in patients suffering from paraquat intoxication. **Materials and Methods:** In this retrospective study, data of 358 patients with acute paraquat poisoning were analyzed in Xi'an, China. The outcome of our study was mortality, and the influential factors were age, gender, marital status, educational level, symptoms at presentation, and laboratory findings. A logistic regression model was utilized to explore the independent risk factors. **Results:** In a total of 358 paraquat-poisoned patients, the significant differences were found between patients who underwent HP and those who did not, particularly regarding mean age (48.02 years vs. 42.32 years; $P = 0.01$), mental disorders (15.6% vs. 6.1%; $P = 0.01$), poisoning severity score (2.36 vs. 2.57; $P = 0.03$), organ failure (10.9% vs. 23.5%; $P = 0.02$), and mechanical ventilation (18.8% vs. 33.3%; $P = 0.02$). Patients who refused HP exhibited a higher mortality (20.3% vs. 10.9%; $P = 0.03$) compared to those who received HP. Age (odds ratio (OR), 1.76; 95% confidence interval (CI): 1.01–3.82; $P = 0.01$) and history of mental disorders (OR, 2.81; 95% CI: 1.19-6.61; $P = 0.02$) were identified as significant independent predictors for the refusal of HP. **Conclusion:** The results of this study showed that elderly individuals and those with a history of mental disorders were independently associated with refusing HP in patients with acute paraquat poisoning.

Key words: Hemoperfusion, mortality, paraquat poisoning, risk factors

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INTRODUCTION

Acute poisoning significantly impacts global public health,[1] resulting in 370,000 deaths annually due to the intentional consumption of large quantities of pesticides.[2] The World Health Organization highlights acute paraquat poisoning as a severe health crisis, particularly prevalent in China, South Asia, and Middle East countries.[3]

Currently, there is no universally accepted treatment regimen for paraquat poisoning, partly due to its widespread availability and underestimation of its dangers.[4] Initial treatment typically involves gastrointestinal decontamination to limit further absorption, often by activated charcoal, although its efficacy in clinical settings remains inadequately supported by high-quality evidence.[5] In recent years, extracorporeal blood purification techniques have gained popularity as vital treatment methods for toxin removal and as supportive therapy.[6] While hemodialysis (HD)

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remains the primary extracorporeal technique in the United States, hemoperfusion (HP) has become more favored in China due to its procedural simplicity, shorter duration, and lower cartridge costs.[7,8]

Previous studies have demonstrated that HP can effectively adsorb and remove paraquat from the blood and eliminate significant amounts of inflammatory mediators.[6,8,9] Despite the documented efficacy of HP in clinical trials for treating paraquat poisoning,[10] a minority of patients remain hesitant to accept this recommended therapy for various reasons.[11] The consequences of refusing HP in paraquat-poisoned patients are severe, with a recent multicenter study revealing a mortality rate of 73.5% among patients who did not undergo HP treatment.[12]

Currently, no studies have specifically explored the factors contributing to the refusal of HP in patients with paraquat poisoning. This research aimed to analyze the comprehensive factors leading to HP refusal and identify high-risk patients. Understanding these aspects could enhance the utilization of HP and aid in developing strategies to improve patient outcomes in cases of paraquat poisoning.

MATERIALS AND METHODS

Study population

Between January 2016 and December 2021, we conducted a retrospective analysis of patients with confirmed acute paraquat poisoning who were requested to utilize HP besides conventional therapy at the Second Affiliated Hospital, Air Force Military Medical University in Xi'an, China. Our hospital is located in the suburban of Xi'an and admits a significant number of patients suffering from acute pesticide poisoning annually.

The study included patients who met the following criteria: (1) exposure to paraquat through oral ingestion; (2) aged between 14 and 79 years; and (3) admission to the hospital within 6 h of poisoning exposure. We excluded patients if they had (1) concurrent poisoning from other drugs or pesticides; (2) with severe underlying conditions such as uremia, cancer, or cardiac diseases; or (3) incomplete data or duplicate cases.

Informed consent was obtained from the patients or, if necessary, their spouses, parents, children, or other relatives who can make a decision for HP treatment. The research protocol and the use of patient data were reviewed and approved by the Research Ethics Committee of the hospital.

Data collection

The enrolled patients were categorized into the Non-HP group and the HP group. The comparison aimed to identify potential risk factors between these groups. Data collected for analysis included: (1) demographics such as age, gender, marital status, place of residence, occupation, and educational level; (2) characteristics of poisoning exposure, medical history, and Poisoning Severity Score (PSS), assessed through vital signs, symptoms at presentation, and laboratory findings; and (3) therapeutic interventions and patient outcomes. Before the analysis, a thorough data examination process was conducted to ensure the accuracy and reliability of the data.

Statistical analysis

Continuous variables following a normal distribution were described as mean ± standard deviation and compared using the Student's unpaired *t*-test. Continuous variables not normally distributed were expressed as median (interquartile range) and assessed using the Mann–Whitney *U*-test. Categorical variables were denoted as case numbers (percentage) and analyzed using the Chi-squared test or Fisher's exact test, depending on the data's appropriateness for each test. A logistic regression model was applied to discern factors independently associated with the refusal of HP. All statistical evaluations were performed using SPSS software (version 24, Chicago, IL, USA), with two-tailed $P < 0.05$ considered statistically significant.

RESULTS

A total of 407 patients with acute paraquat poisoning were initially screened. Following the screening process, 358 eligible cases were ultimately included for analysis, with 64 patients in the non-HP group and 294 patients in the

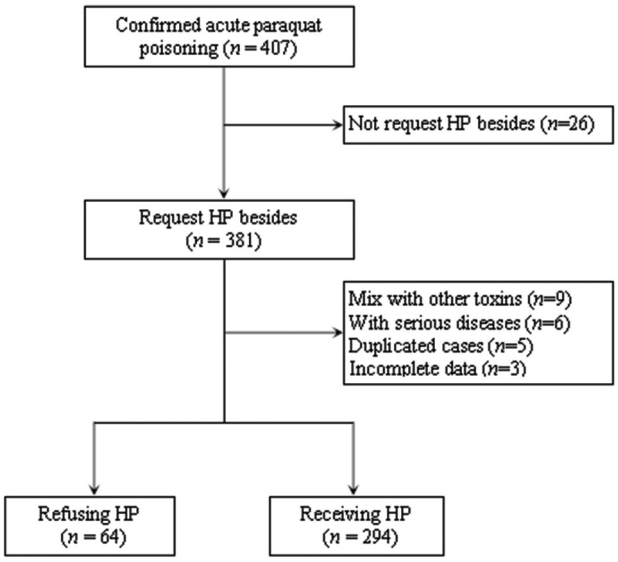

Figure 1: Flowchart of the study. HP = Hemoperfusion

HP group. The patients' inclusion flowchart is depicted in Figure 1.

Demographic characteristics

Demographic variables are compiled and presented in Table 1. No significant statistical differences were observed between the two groups in terms of gender ($P = 0.83$), marital status ($P = 0.64$), residence ($P = 0.54$), occupation ($P = 0.32$), and educational level ($P = 0.84$), respectively. Conversely, individuals who declined HP had a significantly higher mean age (48.02 years vs. 42.32 years; $P = 0.01$) compared to those who accepted HP.

Clinical characteristics

The clinical variables of the included patients are detailed in Table 2. There were no significant differences observed

Table 1: Demographic characteristics of patients with acute paraquat poisoning

Variables/treatments	Non-HP group (*n*=64), *n* (%)	HP Group (*n*=294), *n* (%)	*P*
Age (years), mean±SD (minimum–maximum)	48.02±17.29 (14–78)	42.32±17.01 (14–79)	0.01□
Gender			
Male	34 (53.1)	152 (51.7)	0.83*
Female	30 (46.9)	142 (48.3)	
Marital status			
Single	11 (17.2)	58 (19.7)	0.64*
Married	53 (82.8)	236 (80.3)	
Residence			
Rural	62 (96.9)	276 (93.9)	0.54*
Urban	2 (3.1)	18 (6.1)	
Occupation			
Farmers	42 (65.6)	146 (49.7)	0.32*
Workers	13 (20.3)	78 (26.5)	
Students	5 (7.8)	38 (12.9)	
Unemployed	4 (6.3)	32 (10.9)	
Education level			
Primary school	12 (18.7)	46 (15.7)	0.84*
Middle school	28 (43.8)	122 (41.5)	
High school	17 (26.6)	85 (28.9)	
College	7 (10.9)	41 (13.9)	

*Chi-square test; □Student's unpaired *t*-test. SD=Standard deviation; HP=Hemoperfusion

Table 2: Clinical characteristics of patients with acute paraquat poisoning

Variables/treatments	Non-HP group (*n*=64), *n* (%)	HP group (*n*=294), *n* (%)	*P*
Types of exposure			
Suicide	60 (93.8)	281 (95.6)	0.51*
Accident	4 (6.2)	13 (4.4)	
Poisoning characteristics			
Time to admission (h)	4.0 (3.0–6.8)	4.0 (3.0–6.0)	0.65#
Amount of ingestion (mL)	100 (50–200)	100 (50–200)	0.48#
Serum PQ levels (mg/L)	14.39±11.35 (1.06–30.42)	13.58±11.81 (0.95–38.76)	0.63□
Medical history			
Chronic disease	4 (93.8)	9 (3.1)	0.26*
Mental disorder	10 (15.6)	18 (6.1)	0.01*
Signs and symptoms before HP			
Coma	19 (29.7)	78 (26.5)	0.60*
Shock	3 (4.7)	26 (8.8)	0.26*
Organ failure	7 (10.9)	69 (23.5)	0.02*
Poisoning severity score	2.36±0.82 (1–4)	2.57±0.71 (1–4)	0.03□
Treatments			
Gastric lavage	63 (98.4)	285 (96.9)	1.00*
Mechanical ventilation	12 (18.8)	98 (33.3)	0.02*
Outcomes			
Mortality	13 (20.3)	32 (10.9)	0.03*
Length of stay (h), median (IQR)	31 (12–114)	66 (29–144)	0.00□

*Chi-square test; □Student's unpaired *t*-test; #Mann–Whitney test. PQ=Paraquat; HP=Hemoperfusion; IQR=Interquartile range

between the two groups in suicide (P = 0.51), time to admission (P = 0.65), amount of ingestion (P = 0.48), serum paraquat levels (P = 0.63), chronic disease (P = 0.26), coma (P = 0.60), shock (P = 0.26), and gastric lavage (P = 1.00). The non-HP group had a statistically lower mean PSS compared to the HP group (2.36 vs. 2.57; P = 0.03). In addition, patients who refused HP treatment had a higher incidence of mental disorders (15.6% vs. 6.1%; P = 0.01), a lower incidence of organ failure (10.9% vs. 23.5%; P = 0.02), and less frequent use of mechanical ventilation (18.8% vs. 33.3%; P = 0.02). Furthermore, the mortality was significantly higher in patients who refused HP compared to those who received it (20.3% vs. 10.9%; P = 0.03), and the length of hospital stay was considerably shorter for those refusing HP (31 h vs. 66 h; P = 0.00).

Risk factors

Factors that showed significant differences, such as age, mental disorder, organ failure, PSS, and use of mechanical ventilation, were included in the logistic regression analysis. The result indicated that older age (odds ratio [OR], 1.76; 95% confidence interval [CI]: 1.01–3.82; P = 0.01) and a history of mental disorder (OR, 2.81; 95% CI: 1.19–6.61; P = 0.02) were independently associated with the refusal of HP in addition to standard therapy, as detailed in Table 3.

DISCUSSION

In this retrospective study, we examined the association between various demographic, clinical, and psychological factors and the refusal of HP in patients with acute paraquat poisoning. Our findings identified older age and a history of mental disorders as independent risk factors for HP refusal.

Paraquat, a widely used nonselective herbicide, poses severe health risks such as lung tissue accumulation, free radical formation, alveolitis, and subsequent pulmonary fibrosis, leading to high mortality rates.[13] HP, a blood purification technique that can remove toxins from the blood using adsorbent materials like resins or activated charcoal,[14] is recommended as an effective therapeutic method for paraquat poisoning due to its effectiveness in clearing the blood of toxins.[10,15] Our data revealed a significant reduction in mortality rates among patients treated with HP compared to those receiving only standard care (10.9% vs. 20.3%; P = 0.03), which was in line with the previous studies.[10,12,15] Furthermore, a meta-analysis by Nasr Isfahani *et al*. highlighted that HP treatment significantly reduced mortality (OR: 0.20; 95% CI: 0.10–0.40) in paraquat-poisoned patients compared to conventional therapy alone.[16] In addition, integrating HP with other therapeutic interventions like ulinastatin, Xuebijing, cyclophosphamide, and high-dose ambroxol showed improved survival rates compared to HP treatment alone.[17,18] Despite HP's benefits, the procedure has associated risks, including hypocalcemia, thrombocytopenia, and decreased immunoglobulin levels.[19] Therefore, it is necessary to combine HP with other methods such as HD, continuous venovenous hemofiltration, or continuous renal replacement therapy in certain cases to optimize patient outcomes and mitigate potential complications.[7,20,21]

Table 3: Factors associated with hemoperfusion refusal besides conventional therapy

Variables	OR	95% CI	*P*
Age	1.76	1.01–3.82	0.01
Poisoning severity score	0.72	0.49–1.04	0.78
Organ failure	0.49	0.20–1.67	0.11
Mental disorder	2.81	1.19–6.61	0.02
Mechanical ventilation	0.45	0.22–0.98	0.09

OR=Odds ratio; CI=Confidence interval

Treatment refusal is commonly understood as patients asserting their inherent right to decline certain treatments.[22] In our study, 64 (17.9%) patients opted out of HP treatment and only chose standard therapy, despite recommendations from their physicians. This rate is slightly lower than that reported in previous studies.[12,16] This discrepancy may stem from the rigorous inclusion and exclusion criteria applied in our research. In addition, the factors of age, PSS, mental disorders, organ failure, and mechanical ventilation significantly influenced the refusal of HP treatment among patients with paraquat poisoning, as shown in Tables 1 and 2. These results suggest that older patients, particularly those with a history of mental disorders, were more likely to decline HP treatment due to perceived limited benefits.[23] Conversely, patients experiencing multiple organ failures and requiring mechanical ventilation, conditions considered emergency,were more willing to initiate HP treatment promptly.[24] Moreover, while the PSS is a widely recognized system for assessing a patient's severity and guiding initial treatment decisions,[25] it was frequently misapplied or altered due to unique clinical circumstances.[26] In comparison, the Acute Physiology and Chronic Health Evaluation II score demonstrated superior sensitivity in mortality prediction. Similarly, the Severity Index of Paraquat Poisoning has been shown to be more effective in forecasting the outcomes of patients acutely poisoned by paraquat.[27]

In this study, age and a history of mental disorders were identified as independent risk factors for refusing HP treatment alongside standard therapy, as demonstrated by logistic regression analysis [Table 3]. Previous research had reported that elderly patients were more likely to refuse treatment in situations of severe complications, but they tended to apply treatment more often when different options were explained.[28] Consequently, it is essential to adopt a communication-based approach in which physicians can clearly explain the risks and benefits of HP therapy, outline the consequences of refusing treatment,

respect patients' preferences, and encourage them to voice any specific concerns. In addition, the refusal of treatment by patients with mental disorders should be well-documented and recognized, because it presents ethical and legal dilemmas due to the challenging balance between the patient's right to refuse treatment and the physician's duty to provide care.[29] Overall, considering China's vast cultural and socioeconomic diversity,[30] further researches are warranted to develop more tailored understandings and preventive strategies to enhance patient acceptance of HP in addition to conventional therapy.

Limitations

Several limitations of this study warrant attention. First, the single-center design and the small sample size may limit the generalizability of our findings. In addition, we did not explore other sociodemographic factors, such as monthly income, economic status, and familial relationships, which could influence the refusal of HP treatment. Furthermore, we did not standardize the criteria for HP indication among clinicians, and their individual treatment preferences could have affected patients' decisions regarding HP therapy.

CONCLUSION

Our results indicated that patients who refused HP and only received standard therapy had worse mortality prognosis compared with those who received both of the two therapeutic regimens in acute paraquat poisoning patients. We identified older age and a history of mental disorders as independent risk factors for refusing HP. Future studies with larger sample sizes are warranted to further elucidate this issue.

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Conflicts of interest

There are no conflicts of interest.

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