



A Study on the Role of Hemoperfusion in the Paraquat Induced Acute Renal Failure Patients Attending a Tertiary Care Hospital in Eastern India

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ABSTRACT:

Introduction: Paraquat (PQ), an herbicide, is a very common agent for suicidal, homicidal and accidental poisoning in agriculture based populations. It is easily available, cheap and a highly toxic chemical with high fatality rates in humans. We have studied the use of hemoperfusion in the paraquat induced acute renal failure patients in addition to standard care.

Materials and methods: This is a single centre non blinded study with a 2:1 recruitment in standard (non hemoperfusion) group labeled A and hemoperfusion group labeled B respectively. All patients diagnosed as PQ induced acute renal failure were administered the standard medical care of methylprednisolone 500miligram daily for 3 consecutive days, N acetylcysteine 600 miligram twice daily, and hemodialysis(if serum creatinine was 1.5miligram/deciliter or more/urine output less than 0.5 mililiter per kilogram bodyweight per hour for 6 hours or more /volume overload /metabolic acidosis/hyperkalemia).The baseline characteristics of the patients were studied along with the delay in presentation and the number of sessions of hemodialysis received. Mortality data were collected and analysed.

Results: The baseline characteristics were similar in the two groups. There were 45 patients in group A and 21 patients in group B. Hemoperfusion was given at an average of 2 sessions to 21 patients of group B. None of these 21 patients attended within 4 hours of poisoning.37 patients expired in total. 31 were in the group A and 6 patients were of group B whereas 29 patients survived and were discharged. Of these 14 were in the group A and 15 were in group B. Among the surviving patients, the mean serum creatinine (mean± s.d.) was $2.3690 \pm .9370$ mg/dl ,the mean number of dialysis sessions (mean± s.d.) was 2.5862 ± 1.1501 and the mean time delay in presentation (mean± s.d.) was $1.7931 \pm .4913$ (days). Among the patients who expired, the mean serum creatinine (mean± s.d.) was 4.3514 ± 1.8018 mg/dl, the mean number of dialysis sessions (mean± s.d.) was 2.4865 ± 1.9239 and the mean time delay in presentation was 3.0000 ± 1.1785 (days).

Conclusion: We conclude that charcoal hemoperfusion may improve survival after paraquat ingestion in acute kidney injury patients presenting between 4 to 40 hours. It has been shown to be effective extracorporeal therapy if given within 4 hours of ingestion. Paraquat has almost 100 percent mortality even with hemodialysis. So hemoperfusion may be tried as a last resort in patients presenting within 40 hours as was seen in our study, but further studies are needed.



INTRODUCTION

Paraquat, a bipyridyl herbicide, is a bright green corrosive liquid with pungent smell. It was discovered in 1950s and first marketed in 1962. Presently, it is the second highest-selling weed killer globally and is available in a 20% solution form that needs to be diluted before agricultural use.[1] The main acute systemic effects are pulmonary edema, convulsions, cardiac, renal, and hepatic failure.[2] The LD₅₀ in humans is approximately 35 mg/kg, which translates into as little as 10-15 ml of a 20% solution. Once large concentration of this poison accumulates in lungs or renal cells, it leads to generation of toxic reactive oxygen species through redox cycling, which devastate cellular defensive mechanisms. Renal failure can result due to the direct toxicity and hemodynamic changes. Conservation of renal function is vital to reduce plasma paraquat levels and thereby reduce accumulation in lung cells. Various therapies have been tried like pulse methylprednisolone, cyclophosphamide, N-acetylcysteine, Fullersearth, extracorporeal therapies like hemodialysis and hemoperfusion. None have shown a clear benefit over the others. Timing of extracorporeal therapies has been studied. Some studies have shown beneficial role of charcoal hemoperfusion if given within 4 to 5 hours of poisoning.

Hemoperfusion plays a critical role in managing paraquat-induced acute renal failure, a severe condition resulting from exposure to the herbicide paraquat. Paraquat is known for its high toxicity, leading to oxidative damage and subsequent acute renal failure when ingested or absorbed in significant amounts. In such cases, traditional treatment methods often fall short, necessitating advanced interventions to mitigate systemic toxicity and improve patient outcomes. Hemoperfusion, a technique that involves passing blood through a column containing an adsorbent material to remove toxins, has shown promise in effectively reducing paraquat levels in the bloodstream. This method enhances detoxification by directly adsorbing paraquat and other harmful substances, thereby alleviating renal stress and potentially improving renal function. By reducing the overall toxic burden, hemoperfusion can help stabilize patients and enhance the effectiveness of supportive therapies. This approach, combined with prompt medical intervention and

supportive care, offers a critical advantage in managing the severe effects of paraquat poisoning and improving the prognosis for affected patients.

MATERIALS AND METHODS

This study was conducted in Nil Ratan Sircar Medical College and Hospital, Kolkata in the Department of Nephrology. A total of 72 patients above 12 years of age attended hospital emergency between November 2018 to October 2019 with paraquat poisoning, a herbicide. Patients with mixed poisoning or without documented evidence of paraquat poisoning were not included in the study. Patients with co morbidities like diabetes, chronic obstructive pulmonary disease, malignancies were not included. 5 patients presented within 4 hours of poisoning and did not develop AKI. They were managed as per protocol and were not included in analysis. 1 patient left against medical advice and was excluded. A total of 66 patients were taken up in 2 groups at a ratio of 2:1. Informed consent was taken from all the patient's relatives. It is a single centre study with a 2:1 recruitment in standard (non hemoperfusion) group labeled A and hemoperfusion group labeled B respectively. All patients diagnosed as PQ induced acute renal failure were administered the standard medical care of methylprednisolone 500 milligram daily for 3 consecutive days, N acetylcysteine 600 milligram twice daily, and hemodialysis (if serum creatinine was 1.5 milligram/deciliter or more/urine output less than 0.5 milliliter per kilogram bodyweight per hour for 6 hours or more /volume overload /metabolic acidosis/hyperkalemia). The baseline characteristics of the patients were studied along with the delay in presentation and the number of sessions of hemodialysis received. Mortality data were collected and analysed.

Statistical Analysis:

For statistical analysis data were entered into a Microsoft excel spreadsheet and then analyzed by SPSS 27.0. and GraphPad Prism version 5. Data had been summarized as mean and standard deviation for numerical variables and count and percentages for categorical variables. Two-sample t-tests for a difference in mean involved independent samples or



unpaired samples. Unpaired proportions were compared by Chi-square test or Fischer's exact test, as

appropriate. p -value ≤ 0.05 was considered for statistically significant.

RESULT

Table1: Distribution of Age, Outcome, Combined procedures (Hd +Hp), Sex and Affected Organs

| | | Frequency | Percent |
|------------------------------|----------------------|-----------|---------|
| Age | 11-20 | 29 | 43.9% |
| | 21-30 | 24 | 36.4% |
| | 31-40 | 6 | 9.1% |
| | >40 | 7 | 10.6% |
| | Total | 66 | 100.0% |
| Outcome | Discharged | 29 | 43.9% |
| | Expired | 37 | 56.1% |
| | Total | 66 | 100.0% |
| Combined procedures (Hd +Hp) | No(Group A) | 45 | 68.2% |
| | Yes(Group B) | 21 | 31.8% |
| | Total | 66 | 100.0% |
| Sex | Female | 29 | 43.9% |
| | Male | 37 | 56.1% |
| | Total | 66 | 100.0% |
| Affected Organs | Both Liver + Kidneys | 14 | 21.2% |
| | Lung | 23 | 34.8% |
| | Recovered | 29 | 43.9% |
| | Total | 66 | 100.0% |

Age: In our study, 29(43.9%) patients were in age group 11-20 years, 24(36.4%) patients were in 21-30 years group, 6(9.1%) patients were in the 31-40 years age group and 7(10.6%) patients were >40 years old.

Outcome: In our study, 29(43.9%) patients were discharged from hospital and 37(56.1%) patients had expired.

Combined procedures (Hd +Hp): In our study, 21(31.8%) patients of group B had both hemodialysis and hemoperfusion. 45 patients in group A had only hemodialysis. Both groups received standard inpatient management with methylprednisolone 500 milligram

daily for 3 consecutive days, N acetylcysteine 600 milligram twice daily.

Sex: 29(43.9%) patients were Female and 37(56.1%) patients were Male.

Affected Organs: Above table showed that, 14(21.2%) patients expired with both respiratory and renal failure and 23 (34.8%) patients died due to respiratory failure.

Table 2: Distribution of Mean Age, Total Dialysis sessions, Mortality, Creatinine and Delay

| | Number | Mean | Sd | Minimum | Maximum | Median |
|----------------|--------|---------|--------|---------|---------|---------|
| Age (years) | 66 | 23.5303 | 9.7005 | 11.0000 | 54.0000 | 21.0000 |
| Dialysis (no.) | 66 | 2.5303 | 1.6193 | 0.0000 | 9.0000 | 2.0000 |



| | | | | | | |
|---------------------------|----|--------|--------|--------|---------|--------|
| Mortality (days) | 37 | 5.9189 | 4.7398 | 1.0000 | 22.0000 | 4.0000 |
| Creatinine (mg/dl) | 66 | 3.4803 | 1.7774 | 1.5000 | 7.8000 | 3.1000 |
| Delay (days) | 66 | 2.4697 | 1.1124 | 1.0000 | 5.0000 | 2.0000 |

Age: Above table showed that the mean age of patients was 23.5 years with a minimum age for suicidal poisoning being 11 years.

Total Dialysis sessions: Our study showed that the mean number of Dialysis sessions given was 2.5303 ± 1.6193 .

Mortality: Above table showed that the mean day of death was 5.9189 ± 4.7398 days

Creatinine: Our study showed that that the mean creatinine at presentation was 3.4803 ± 1.7774 with a maximum of 7.8 mg/dl.

Delay: The mean time delay between poisoning and admission was 2.46 days.

Table 3: Association between Age Combined procedure (HD +HP), Sex and Affected Organs

| | | Discharged | Expired | Total | Chi-Square Value | P-Value |
|-----------------------------------|-------------------------|------------|---------|-------|------------------|---------|
| Age | Nov-20 | 15 | 14 | 29 | 3.7388 | 0.2911 |
| | 21-30 | 8 | 16 | 24 | | |
| | 31-40 | 4 | 2 | 6 | | |
| | >40 | 2 | 5 | 7 | | |
| | Total | 29 | 37 | 66 | | |
| Combined procedure Hd + Hp | No | 14 | 31 | 45 | 9.4485 | 0.0021 |
| | Yes | 15 | 6 | 21 | | |
| | Total | 29 | 37 | 66 | | |
| Sex | Female | 15 | 14 | 29 | 1.2727 | 0.2592 |
| | Male | 14 | 23 | 37 | | |
| | Total | 29 | 37 | 66 | | |
| Affected Organs | Both Kidney+lung | 0 | 14 | 14 | 66 | <0.0001 |
| | Lung | 0 | 23 | 23 | | |
| | No | 29 | 0 | 29 | | |
| | Total | 29 | 37 | 66 | | |

Age

In Discharged group, 15 (51.7%) patients were 11-20 years old, 8 (27.6%) patients were 21-30 years old, 4 (13.8%) patients were 31-40 years old and 2 (6.9%) patients were >40 years old.

In Expired group, 14 (37.8%) patients were 11-20 years old, 16 (43.2%) patients were 21-30 years old, 2 (5.4%)

patients were 31-40 years old and 5 (13.5%) patients were >40 years old.

Association of Age In Group vs Group was not statistically significant ($p=0.2911$).

Combined procedure (Hd+ Hp)

In Group B who received combined procedures of hemodialysis and hemoperfusion, 15 patients out of



total 21 recovered and 6 patients expired whereas in Group A, 31 out of 45 patients who did not receive hemoperfusion expired and 14 survived. It was statistically significant ($p=0.0021$).

Sex

In Discharged group, 15 (51.7%) patients were female and 14 (37.8%) patients were male.

In Expired group, 14 (48.3%) patients were female and 23 (62.2%) patients were male.

Association of Sex vs Group was not statistically significant ($p=0.2592$).

Cause

Among patients who expired, 23 (62.2%) patients died due to Lung involvement and 14 patients had both respiratory and renal failure. 29 patients who recovered did not have lung involvement. They had acute kidney injury at presentation. 14 patients were from group A who received standard therapy including hemodialysis. 15 patients were from group B who received hemoperfusion along with standard therapy with hemodialysis.

Association of death in patients who developed respiratory failure with or without acute renal injury was more than patients without respiratory involvement. It was statistically significant ($p<0.0001$).

Table: Distribution of Mean Age, number of dialysis sessions, serum creatinine at presentation and delay in presentation: outcome

| | Outcome | Number | Mean | Sd | Minimum | Maximum | Median | P-Value |
|-------------|------------|--------|---------|---------|---------|---------|---------|---------|
| Age | Discharged | 29 | 22.1034 | 9.1587 | 12.0000 | 48.0000 | 19.0000 | 0.2936 |
| | Expired | 37 | 24.6486 | 10.0863 | 11.0000 | 54.0000 | 23.0000 | |
| Dialysis | Discharged | 29 | 2.5862 | 1.1501 | 0.0000 | 5.0000 | 3.0000 | 0.8061 |
| | Expired | 37 | 2.4865 | 1.9239 | 0.0000 | 9.0000 | 2.0000 | |
| Creatinine | Discharged | 29 | 2.3690 | .9370 | 1.5000 | 4.6000 | 2.0000 | <0.0001 |
| | Expired | 37 | 4.3514 | 1.8018 | 1.7000 | 7.8000 | 4.1000 | |
| Time (Days) | Discharged | 29 | 1.7931 | .4913 | 1.0000 | 3.0000 | 2.0000 | <0.0001 |
| | Expired | 37 | 3.0000 | 1.1785 | 1.0000 | 5.0000 | 3.0000 | |

Age

In Discharged group, the mean Age (mean \pm s.d.) of patients was 22.1034 \pm 9.1587.

In Expired group, the mean Age (mean \pm s.d.) of patients was 24.6486 \pm 10.0863.

Distribution of mean Age with outcome was not statistically significant ($p=0.2936$).

Dialysis

In the Discharged outcome group, the mean number of dialysis sessions (mean \pm s.d.) of patients was 2.5862 \pm 1.1501.

In the Expired outcome group, the mean number of dialysis sessions (mean \pm s.d.) of patients was 2.4865 \pm 1.9239.

Distribution of mean number of dialysis sessions with outcome was not statistically significant ($p=0.8061$).

Creatinine

In the Discharged outcome group, the mean creatinine (mean \pm s.d.) of patients was 2.3690 \pm .9370.

In the Expired group, the mean Creatine (mean \pm s.d.) of patients was 4.3514 \pm 1.8018.

Distribution of mean Creatine with outcome was statistically significant ($p<0.0001$).

Time (D)

In Discharged group, the mean time after poisoning in days was 1.7931 \pm .4913 (days).

In Expired group, the mean time after poisoning in days was 3.0000 \pm 1.1785 (days).

Distribution of mean time delay with outcome was statistically significant ($p<0.0001$).



DISCUSSION

PQ is a well-known herbicidal poison. It is cheap and easily available in the agricultural belts of Asian countries. Therefore it is a common cause for suicidal and accidental poisonings. Retrospective data over last 5 years of our tertiary care hospital in Eastern India have shown near to hundred percent mortality in cases of PQ poisonings. We studied the efficacy of in vitro charcoal hemoperfusion in addition to standard medical care in such cases. A total of 66 patients of PQ poisoning attending the hospital emergency were studied. 21 patients underwent HP in addition to standard care. 15 patients recovered and were discharged without any pulmonary complications by 28 days of hospital stay. 6 patients expired despite receiving HP. 45 patients received standard medical care with methylprednisolone, N acetylcysteine and hemodialysis. Of them 14 patients survived and 31 patients expired.

Demographic indices

Hsu CW et al [3] (2019) showed that thousands of paraquat (PQ)-poisoned patients continue to die, particularly in developing countries. All patients were suicidal cases that had ingested a 24% liquid PQ concentrate. The mean age was 39.3 ± 16.1 years and the median age was 36 years (minimum: 18 years; maximum: 79 years); most of the patients were young and healthy.

In our study 29 patients (43.9%) were in the age group 11-20 years, 24 patients were in the age group of 21-30 years. 37 patients were male and 29 patients were female.

Clinical indices: Mortality owing to respiratory failure alone was 62.2% (23 patients). In addition to this, 14 patients had both respiratory and renal failure at the time of death. Sharma DS et al [4] (2019) found that Our patient presented with above lethal dose intake of paraquat containing substance and we did gastric lavage followed by charcoal hemoperfusion and hemodialysis but patient could not be saved despite optimum efforts suggesting the high fatality of this kind of poisoning. Association of death with development of respiratory failure was significant ($p < 0.0001$). The age of patients, gender or the number of hemodialysis sessions were not significantly associated with increased mortality.

However the delay in presentation to hospital was significantly associated with poor outcome.

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Conflict of interest: None to declare

CONCLUSION

In conclusion, hemoperfusion represents a valuable therapeutic option for managing paraquat-induced acute renal failure, offering a critical advantage in the detoxification process. By effectively adsorbing paraquat from the bloodstream, hemoperfusion helps to mitigate the systemic toxicity and reduce the renal burden associated with paraquat poisoning. This intervention can stabilize patients and potentially improve renal function, especially when used in conjunction with other supportive treatments. The role of hemoperfusion underscores the need for prompt and targeted approaches in the management of severe paraquat toxicity, highlighting its potential to enhance patient outcomes and provide a crucial line of defense against the devastating effects of paraquat-induced renal injury.

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