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RESEARCH ARTICLE

Evaluation of the effect of hemodialysis on paraquat poisoning in patients in a Tertiary Care Hospital, West Bengal, India: A cross-sectional study

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ABSTRACT

Background: Among the class of organophosphates, paraquat remains the commonly used herbicidal compound for self-poisoning in developing countries. Ingestion of paraquat is a leading cause of fatal poisoning in many parts of the world. The absence of any standard guidelines on the treatment of patients with paraquat self-poisoning remains an area of scientific research. The treatment varies from various combinations of immune-modulation, antioxidant therapy, hemoperfusion, and hemodialysis (HD). **Aims and Objectives:** The present study was undertaken to evaluate the role of early initiation HD in the determination of prognosis in the case of paraquat poisoning. **Materials and Methods:** This cross-sectional study was conducted on the patients suffering from paraquat poisoning, attending the Medicine ward of R. G. Kar Medical College, Kolkata. The patients were subjected to HD and blood was collected before and after therapy. Demographic characteristics of the patients, mortality rate, hepatic, and renal markers in serum were estimated. **Results:** In the present study, 61 patients with paraquat poisoning were considered following all the inclusion and exclusion criteria. Of 61 patients, 16 patients (26.2%) survived 2 weeks of hospital stay, whereas 45 (73.8%) patients expired. Among the survivors, the mean value of the day of starting dialysis was 1.13 days in contrast to 2 days among the non-survivors. These data showed a significant correlation with mortality with $P < 0.0001$. **Conclusion:** The present study, thus, highlighted the fact that early detection and immediate therapeutic action can reduce the risk of mortality in patients suffering from paraquat poisoning.

KEY WORDS: Hemodialysis; Paraquat; Poisoning; Tertiary Care

INTRODUCTION

Self-poisoning with pesticides is one of the major public health issues in developing countries. It is estimated that 3,00,000 deaths occur in the Asia–Pacific region alone each year for pesticide poisoning.[1,2] In Sri Lanka, 300–400 deaths occur due to self-poisonings with pesticides each year.[3,4] One of the major used herbicide is paraquat. This is because it is a rapidly acting, nonselective nature and is relatively inexpensive. These characteristics contribute to its widespread use in developing countries. Paraquat is reasonably safe to use in agriculture which may cause dermal or localized injury. However, accidental or deliberate ingestion has an extremely high case-fatality rate. Largely for this reason, paraquat has been restricted in many parts of the world. In countries where it remains readily available, it is a common method for intentional self-poisoning. Paraquat ingestion is a leading cause of fatal poisoning in many parts of Asia, Pacific Nations, and the United States of America.[5,6]

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Researches have shown that in between the year 1986 and 1990, 63% of all suicide deaths in Trinidad and Tobago were due to paraquat ingestion. A similar study in South Trinidad (between 1996 and 1997) and Samoa (between 1979 and 2000) reported that 76% and 70% of the total suicides were due to paraquat injection, respectively.[7,8] Between 1945 and 1989, paraquat was responsible for 56% of all pesticide deaths in England and Wales.[9,10] Paraquat ingestion was held responsible for most of the deaths in the American Association of Poison Control Centers' National Poison Data System in the year 2008.[11] In Sri Lanka, there have been trials of new formulations to reduce toxicity of the paraquat formulation. It is reported that the new formulations have had only very modest effects on fatality.[12,13]

The very high case fatality of paraquat is due both to its inherent toxicity and the lack of any effective treatment. There are no widely accepted guidelines on treatment of patients with paraquat self-poisoning. The treatment varies from supportive care alone to various combinations of immune-modulation, antioxidant therapy, hemoperfusion, and hemodialysis (HD). However, the overall mortality remains >50% in centers routinely practicing such intensive measures. Furthermore, these treatment options have been largely based on extrapolation of evidence from animal studies. Despite the lack of strong evidence or consistent recommendations, any rational approach for the treatment of paraquat poisoning should consider both the mechanism of toxicity and toxicokinetics of paraquat. The present study was undertaken to evaluate the role of early initiation HD in the determination of prognosis in the case of paraquat poisoning.

MATERIALS AND METHODS

Place of Study

The study was carried out in the Medicine ward of R. G. Kar Medical College and Hospital, Kolkata, West Bengal, India.

Study Duration

Ethical clearance

Ethical clearance was obtained from Institutional Ethics Committee, R. G. Kar Medical College, Kolkata, before initiation of the study.

Inclusion criteria

Patients between 15 years and 60 years of age with relevant history and signs/symptoms of paraquat poisoning were included in the study.

Exclusion criteria

The following exclusion criteria were excluded from the study:

- Patients with a history suggestive of prior kidney/liver disease
- Immunocompromised patients
- Patients with history of suicidal intake of other poisons/ medication along with paraquat.

Methodology

This was a cross-sectional study. Patients admitted in the hospital with signs and symptoms of paraquat poisoning following inclusion and exclusion criteria were considered for the present study. Demographic features of the patients were documented. Before therapy, blood was collected from these patients for evaluating hepatic and renal biomarkers – aspartate aminotransferase (AST), alanine aminotransferase (ALT), urea, and creatinine. All the patients were subjected to HD and after HD, blood was again collected for estimating the hepatic and renal biomarkers. The patients were admitted in the hospital for a period of 2 weeks and the mortality rate was evaluated. The patients who died during the follow-up period were designated as expired patients and the patients who were alive were designated as survived patients for the present study.

RESULTS

In the present study, 61 patients with paraquat poisoning were considered for the present study following all the inclusion and exclusion criteria. Among the 61 patients, 40 patients (65.57%) were male and 21 patients (34.43%) were female [Figure 1]. The mean age of the patients was 31.11 years. Of 61 patients, 16 patients (26.2%) survived 2 weeks of hospital stay, whereas 45 (73.8%) patients expired. The mean distribution of age among the patients who expired was found to be 30.96 ± 5.97 years. Among the survived patients, the age distribution was found to be 27.66 ± 7.85 years. The result indicated that the difference of mean age versus outcome was not statistically significant (P = 0.1544). Among the male population of 40 patients, 33 patients expired, and 7 patients survived, whereas among the female population of 21 patients, 12 patients expired, and 9 patients survived [Figure 1].

The present study revealed that 9 patients received HD on the day of taking paraquat, i.e. within 24 h of ingestion of paraquat and 40 patients received HD within 24 h–48 h. The rest of 12 patients, due to late admission in our hospital, received hemodialysis after 48 h.

Among the survivors, the mean value of the day of starting dialysis was 1.13 days in contrast to 2 days among the non-survivors. These data showed a significant correlation with mortality with $P < 0.0001$.

Before receiving HD, the mean AST concentration in blood was 38.38 ± 9.008 U/L among the patients, included in the present study. After receiving HD, the mean AST concentration in blood was found to be 71.24 ± 9.89 U/L in the patients, who expired during the follow-up period and 68.87 ± 8.71 U/L in the survived patients [Figure 2]. A similar elevation in ALT

level was observed in the patients before and after HD. In the present investigation before receiving HD, the mean ALT concentration in blood of the patients was 41.64 ± 10.39 U/L. However, after receiving HD, the mean ALT concentration in blood was 74.66 ± 3.66 U/L in the expired patients and 73.06 ± 4.59 U/L in the survived patients [Figure 2].

Estimating urea in patient samples before receiving HD revealed that, the mean concentration in blood was 46.34 ± 14.01 mg/dL. Post-HD, the mean urea concentration in blood was measured to be 71.31 ± 18.15 mg/dL for the expired patients and 57.56 ± 10.29 mg/dL in the survived patients [Table 1]. Creatinine concentration in patient samples, before receiving HD, was 1.99 ± 0.59 mg/dL. However, decreased level of creatinine was evident in both the expired patients (1.49 ± 0.32 mg/dL) as well as the survived patients (1.36 ± 1.04 mg/dL), as shown in Table 1.

Table 1: Concentration of urea and creatinine in the blood of the patients

Parameters	Survived patients	Expired patients
Concentration of urea in blood (mg/dl)	71.31±18.15	57.56±10.29
Concentration of creatinine in blood (mg/dl)	2.27±0.33	1.72±1.04

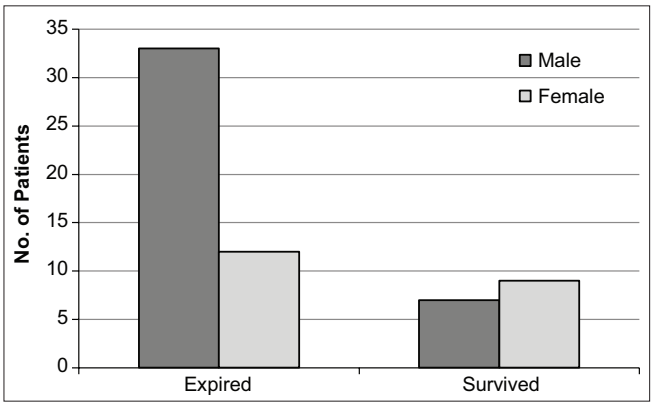

Figure 1: Gender distribution of the survivor and the expired patients in the present study

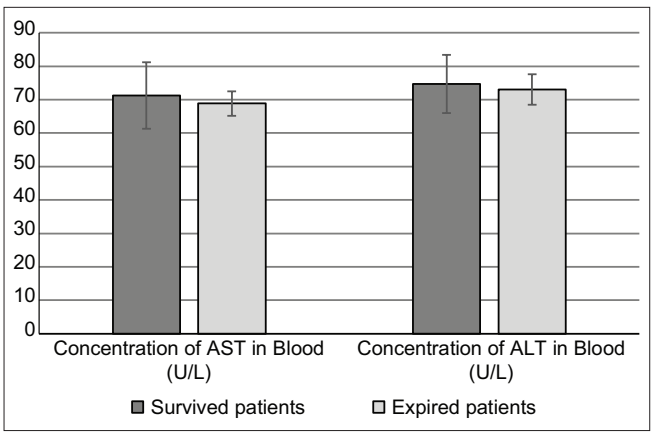

Figure 2: Concentration of aspartate aminotransferase and alanine aminotransferase in the blood of the patients

DISCUSSION

Paraquat (1,1′-dimethyl-4, 4′-dipyridylium) is a broad-spectrum herbicide that results in severe toxicity due to accidental or intentional administration in the human body. Paraquat is known to cause renal, hepatic, and lung injury in patients suffering from paraquat poisoning.[14] HD is among the most common treatment of paraquat poisoning. The present study tried to estimate the rate of mortality and level of various biochemical markers of the patients admitted in the tertiary care hospital due to paraquat poisoning. Results from the present study opined that delay in the onset of HD was a major drawback in the treatment of the patients suffering from paraquat poisoning. Biomarkers of liver and kidney were also perturbed before and after HD. This indicated a possible cause of the increased mortality of such patients.

Sixty-one patients, included in the present study, suffered from paraquat poisoning and they received HD immediately after admission in the hospital. About 65.57% of these patients were male and rest 34.43% were female. This result was in accordance with another study in South India, where 80% of the patients were male.[15] The age of the patients in the present study ranged from 16 to 46 years. The mean age of the study population was 30.11 years. A retrospective study in Karnataka also revealed most of the patients belonged to the age group of 30–40 years.[16] Among the 61 participants, 26.2% survived during 2 weeks of hospital stay, whereas 73.8% expired during the tenure. However, mortality rate was found to be 100% in the study conducted in Tamil Nadu.[15] Another cross-sectional study by Thunga *et al*. reported a mortality rate of 61.7%. Mean age of the survivors was 27.67 years, whereas that of the expired was 30.96 years. About 82.5% of the male patients expired whereas, 57.14% of the female patients expired.[17] In the present study, 9 of the 61 participants received HD within 24 h, 40 received HD within 24–48 h, however, due to late admission, 12 patients received the treatment after 48 h. Delay in the initiation of the treatment was found to be correlated with the rate of mortality. The patients receiving treatment within 24 h had a better chance of survival. This observation was supported by the study conducted by Rao *et al*., where it was observed that the survival rate was higher for the patients who underwent hemoperfusion in ≤6 h compared to those who received hemoperfusion therapy after 6 h.[18] Aminotransferases, ALT, and AST are enzymes that catalyze the transfer of α-amino groups from alanine and aspartate to the α-keto group of ketoglutaric acid to generate pyruvic and oxaloacetic acids, respectively. These aminotransferases are highly concentrated in liver. Any kind of liver injury will lead to excess amount of these enzymes in the serum. Therefore, AST and ALT are enzymes in serum that act as biomarkers for the estimation of hepatic injury.[19] These two parameters were estimated before and after HD. It was found that AST level in serum was increased by 85.62% in the expired patients before and after therapy. However, the increase was found to be 79.44% for the survived patients. ALT levels in serum were also increased by 79.3% and 75.45% in expired

and survived participants, respectively. Thus, HD was found to be associated with a rise in these levels. Urea is an end product of amino acid metabolism produced in the liver and excreted by the kidney. Creatinine is the product produced by the breakdown of creatine phosphate in muscles. Creatinine is also removed from the human body by the kidney. Therefore, any kind of renal impairment will lead to enhanced levels of these end products. Thus, urea and creatinine are used as biomarkers for renal injury.[20] The present study estimated the urea levels before and after therapy. Urea level was found to be increased by 1.54 fold and 1.24 fold in the expired and survived patients, respectively. Creatinine level in the expired participants diminished by 25.12% after HD. However, the reduction in the creatinine level among the survived patients was 31.66%. As a result of this physiological stress, HD patients often suffer from compromised quality of life.[21]

Epidemiological study regarding the treatment of paraquat patients is limited, especially in the Eastern zone of the country. The present study, therefore, evaluated the treatment procedure and rate of mortality of the patients suffering from paraquat poisoning. Sample size of the present study is major limitation. Few other biochemical parameters also need to be estimated to reduce the rate of mortality. Psychological condition of the patients could not be recorded which might contribute to a major cause of mortality.

CONCLUSION

Paraquat poisoning often has fatal consequences in patients. Management of paraquat poisoning remains a challenge for the physicians till date. The present study tried to estimate the rate of mortality of patients suffering from paraquat poisoning and its correlation with the time of onset of HD. The hepatic and renal biomarkers were also evaluated before and after therapy. Early diagnosis and immediate treatment is thus of utmost importance in combating paraquat poisoning.

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