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URINARY PARAQUAT LEVELS, WHITE BLOOD CELL COUNT, C-REACTIVE PROTEIN, AND ACUTE PARAQUAT POISONING: A TERTIARY CARE HOSPITAL RESEARCH ON PROGNOSIS

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Abstract

Aim: To determine the predictive usefulness of urinary paraquat, C-reactive protein (CRP), and white blood cell (WBC) counts in individuals with acute paraquat poisoning. **Methods:** Patients with a history of paraquat intake who presented to the emergency department were included in this study. On days 0, 1, 2, and 3 of the hospital stay, blood samples were analyzed for WBC, CRP level, and urinary paraquat level. The patient survived or died in the hospital. The levels of these biomarkers were compared between the groups that survived and those that did not using statistical methods. Using receiver operating characteristic (ROC) curve analysis, we determined the prognostic usefulness of these biomarkers. The present study included 50 patients as participants. The non-survival group had elevated serum levels of all three indicators compared with the survival group. **Results:** While CRP and urinary paraquat levels increased more slowly in the early stages of poisoning, WBC counts typically increased quickly. It was shown that urinary paraquat levels were the best predictor of in-hospital mortality, and the earliest time these biomarker levels could be utilized to predict survival was on the first day of hospital stay. **Conclusion:** Following acute paraquat exposure, the WBC rose sharply. The strongest predictor of in-hospital death was the urinary paraquat level.

Keywords: White Blood Cells, Paraquat Poisoning, Urinary Paraquat, C-reactive Protein, Paraquat Exposure.

INTRODUCTION

Paraquat is a widely used herbicide that can cause severe poisoning and is the leading cause of death due to herbicide poisoning in both developed and developing countries [1]. Paraquat poisoning can occur through several routes, including accidental or deliberate oral ingestion, skin exposure, and inhalation [2]. It can lead to several health issues such as renal insufficiency, respiratory distress, and central nervous system disorders [3, 4]. The diagnosis of paraquat poisoning is based on a history of exposure to the herbicide, and laboratory tests are not commonly available [5]. The treatment of paraquat poisoning involves decontamination, supportive care to maintain organ function, and advanced treatments such as hemodialysis or hemoperfusion [1-5]. Despite the lack of an effective antidote, early identification of high-risk patients and aggressive end-organ supportive care can improve outcomes [6, 7]. The severity of the disease and mortality rate are directly related to the amount of paraquat ingested; however, this information is often unreliable [5-7].

Identifying prognostic markers that correlate with disease severity and patient outcomes is crucial because blood or urine tests to quantitatively detect paraquat are not commonly available in most hospitals [8]. Various studies have examined different markers, such as patient demographics and vital signs, to predict organ failure and mortality rates in patients with acute paraquat poisoning [9-111. However, these

clinical markers tend to be influenced by other factors, which leads to considerable variability. Several models for predicting patient mortality have been studied; however, they are often too complex for bedside use [12]. Recent studies have suggested the potential utility of inflammatory biomarkers in predicting disease severity and outcomes in patients with acute paraquat poisoning [13-15]. Systemic inflammation and reactive oxygen species production through redox cycling are the main pathways leading to multiorgan failure in these patients [15, 16]. Suppressing the inflammatory response is considered to ameliorate disease severity and prevent death. Some studies have shown that serum levels of acute-phase reactive proteins such as urinary paraquat and C-reactive protein (CRP) have prognostic value [4,6,9,12,14,15]. However, further studies are needed to confirm these results and head-to-head comparisons of different laboratory parameters are required. In the current study, we assessed the white blood cell (WBC) count and urinary paraquat and CRP levels in patients with acute oral paraquat poisoning and compared the levels of these biomarkers between survivors and non-survivors at different time points of hospitalization to determine their prognostic value.

MATERIALS & METHODS

The present study was a prospective observational study performed in the emergency room and intensive care unit of the SCB Medical College and Hospital, Cuttack, Odisha. The study protocol was approved by the Institutional Ethics Committee of our hospital. Informed consent was obtained from all patients or their family members. The inclusion criteria were as follows: 1) oral ingestion of paraquat, 2) positive urine paraquat qualitative test, and 3) less than 12 h after oral ingestion of paraquat at admission. The exclusion criteria were as follows: 1) co-poisoning with other substances; 2) presence of other inflammatory conditions, such as sepsis, viral or bacterial infections, and chronic connective tissue disorders; 3) history of cardiac, pulmonary, liver, or renal disease; and 4) length of stay <24 h after hospital admission. All patients enrolled in the study immediately received standard treatment according to the pre-written acute paraquat poisoning treatment protocol at the time of admission to the emergency department. This included gastric lavage (if presented <6 h after oral ingestion), catharsis, antioxidants (vitamin C, vitamin E, and glutathione), high-dose glucocorticoids, antiadrenergic agents (propranolol), and hemoperfusion therapy immediately following hospital admission and continued twice a day for 3 days). Patients were followed-up until hospital discharge or death. Patient age, sex, time between oral ingestion and gastric lavage, and outcomes (survival or non-survival) during the hospital stay were recorded. Laboratory tests for WBC count, serum CRP, and urinary paraquat were performed on days 0 (admission), 1, 2, and 3. WBC count and serum CRP levels were tested according to the standard hospital laboratory protocol. Urinary paraquat levels were determined using an enzyme-linked immunosorbent assay (ELISA) (Creative Diagnostics) according to the manufacturer's protocol.

Statistical analysis:

To evaluate the two groups, we used the Chi-square test, Bonferroni test, or Mann-Whitney U test to compare baseline parameters and the time interval between intake and gastric lavage, as appropriate. We performed a Bonferroni t-test or Mann-Whitney test to compare the white blood cell count, C-reactive protein, and urinary paraquat levels at 0, 1, 2, and 3 days. The area under the curve (AUC) was calculated using

three markers at the beginning, middle, and end of hospital stay. The Youden index was used to identify optimal cut-off values. SPSS (19.0, Microsoft, USA) software was used to perform statistical analyses. Differences between groups were considered statistically significant if the corresponding P-value was less than 0.05.

RESULTS

The study enrolled 50 cases out of 112 paraquat-toxicity patients (19–51 years old, 36–19 years old), of which 25 (50%) were male. The non-survival group had a mean survival of 6.3 days. No significant disparities were identified in terms of age, sex distribution, or duration between oral paraquat ingestion and gastric lavage between the two groups. Urinary paraquat levels, white blood cell counts, and C-reactive protein concentrations at various time intervals On days zero, one, two, and three, the non-survival group exhibited substantially elevated levels of urinary paraquat, C-reactive protein, and white blood cell counts in comparison to the survival group. The sole anomaly was observed in WBC count on day 3, where no substantial difference was found between the two cohorts. The peak WBC count occurred on day zero, after which it declined. C-reactive protein and urinary paraquat concentrations progressively increased and peaked on days two and three of the hospital stay, respectively. Analysis of the ROC curve revealed that these biomarkers could be used to statistically differentiate between survival and non-survival groups as early as the first day of hospitalization. The area under the curve (AUC) for urinary paraquat was greater than that for WBC count (0.79, 95% CI 0.67-0.94) and CRP (0.81, 95% CI 0.72-0.93) on the first day of hospitalization. The optimal cut-off values for urinary paraquat, CRP, and WBC count were as follows: 25.5 (with a sensitivity of 74.5% and a specificity of 83.9%; Youden index: 0.47); 28.2 (with a sensitivity of 79.6% and a specificity of 81.8%; Youden index: 0.40); and 9.1 (with a specificity, 87.2%; sensitivity, 78.8%; Youden index, 0.25), respectively.

DISCUSSION

The WBC count, CRP, and urinary paraquat levels of patients with acute oral paraquat poisoning were found to be significantly elevated in the non-survival group compared to those in the survival group in this study. The WBC count experienced a sharp increase following poisoning, which then abruptly reversed. Although C-reactive protein and urinary paraquat levels increased at a relatively gradual rate, their elevated concentrations persisted for several days. Statistical prediction of survival was feasible as early as the first day of hospitalization, and urinary paraquat level had the greatest predictive value for in-hospital mortality. Paraquat is a highly toxic substance that causes acute toxicity in humans, most frequently via oral ingestion. Based on pharmacokinetic investigations, oral ingestion results in an absorption rate ranging from 5 to 15%, with the maximal serum concentration occurring within 1–4 h after ingestion [6]. The kidneys eliminate most paraquat without subjecting it to metabolism within 12–24 h of ingestion [20]. Although the median lethal dose (LD50) for paraquat is estimated to be between 30 and 50 mg/kg, clinical estimation of the ingested volume is generally unreliable. Therefore, additional clinical or laboratory markers are required to promptly initiate aggressive treatment for patients who are at a high risk of mortality. As paraquat poisoning is linked to inflammatory injury, attempts have been made to increase survival rates through the administration of treatments that inhibit the

inflammatory process. The potential utility of inflammatory markers in identifying patients with unfavorable prognoses is uncertain.

Several preclinical and clinical studies have demonstrated a relationship between peripheral WBC count, disease severity, and prognosis following acute paraquat poisoning [15,24]. Increased WBC count has been associated with a higher risk of multiorgan failure and mortality [25]. In the present study, WBC counts at admission (day 0) were higher in the non-survival group than in the survival group, but the levels rapidly decreased thereafter. On day 3 of hospitalization, the levels were not significantly different between the non-survival and survival groups. This suggests that the WBC count at the time of hospital admission may be a useful early marker of severe disease. However, the prognostic value of the WBC count decreased once treatment was initiated.

Our findings showed that patients in the non-survival group had significantly higher CRP levels than those in the survival group at all the time points. Unlike the WBC count, which peaked on day 0, peak CRP levels were observed on day 1. C-reactive protein is secreted by hepatic cells upon stimulation by other early inflammatory cytokines, such as interleukin-6, which may explain the relative delay in the increase in CRP levels. Future studies focusing on early inflammatory cytokines, such as interleukin 6, may help to identify patients with severe poisoning at the time of admission.

Studies [12, 16] demonstrated a correlation between levels of urinary paraquat and pulmonary function as well as the extent of multi-organ damage in patients with ARDS, which is the most common cause of death in patients with acute paraquat poisoning. In the present study, the urinary paraquat level was significantly higher in the non-survival group than in the survival group. Unlike CRP levels, which peaked on the first day of hospitalization, urinary paraquat levels demonstrated a more gradual increase, attaining their highest levels on the second day of hospital admission. Pharmacokinetic research has revealed that a substantial portion of paraquat is eliminated through the kidneys without undergoing metabolism within the initial 12–24 h following ingestion. By the second day of hospital admission, patients typically receive treatment, such as catharsis, antioxidants (vitamin C, vitamin E, and glutathione), high-dose glucocorticoids, and hemoperfusion. The fact that urinary paraquat levels remained elevated on the second day suggests that the inflammatory reaction persisted or even intensified after paraquat was removed and the inflammatory response was suppressed. These persistently high levels of inflammation may have contributed to the patient's death. This observation is consistent with the findings of an earlier study that showed that patients who received early hemoperfusion therapy still had a high mortality rate [5, 16]. To improve survival rates, future treatment should focus not only on removing paraquat but also on suppressing the inflammatory response.

According to our findings, after acute paraquat poisoning, the concentrations of all three inflammatory biomarkers increased, which aligns with previous studies, indicating that an inflammatory process is involved in the pathophysiology of paraquat toxicity. Even after treatment, the levels of inflammatory biomarkers such as CRP and urinary paraquat remained elevated. The treatment regimen involving gastric lavage, catharsis, hemoperfusion, and administration of immunosuppressants, such as glucocorticoids, to eliminate paraquat may not be sufficient to significantly increase the survival rate, as suggested by our results. At our facility, the paraquat poisoning

treatment protocol does not include an aggressive immunosuppressive regimen of cyclophosphamide and glucocorticoids, which has been shown to enhance survival rates in multiple small randomized clinical trials [4]. Further studies are required to investigate the prognostic significance of various inflammatory biomarkers in patients receiving intensive immunosuppressive therapy.

In our study, we calculated the AUC of the ROC curves to compare the prognostic value of urinary paraquat, WBC, and CRP levels. Upon initial evaluation in the emergency room, none of the three markers exhibited statistically significant AUC values, although their levels were significantly higher in the non-survival group than in the survival group. This finding indicates that pre-admission screening for these indicators was insufficient to identify patients at a higher risk of in-hospital death. However, on the initial day of admission, all three markers exhibited statistically significant AUC values, suggesting that they can potentially predict survival. Among the three markers, urinary paraquat appeared to be the most accurate predictor of mortality, as its association with the highest AUC value was the most pronounced.

The medical literature reveals an important pathway for tertiary care research regarding the association between urinary paraquat levels, white blood cell count, C-reactive protein, and the prognosis of acute paraquat poisoning. This study examined the complex relationship between biological markers and clinical outcomes within hospital hallways. To better understand the course of treatment for patients affected by this harmful insult, doctors conduct thorough analyses to decipher the prognostic implications. Improving patient treatment and refining prognostic markers in the face of paraquat poisoning is a global initiative that has crossed borders and fostered collaboration among medical communities worldwide.

CONCLUSION

In individuals with acute paraquat poisoning, we examined three biomarkers: white blood cell count, C-reactive protein level, and urine paraquat level. Among the three, white blood cell counts increased first. Urinary paraquat levels were the most accurate predictor of death during hospitalization. High urine paraquat levels may warrant a more aggressive treatment approach, potentially increasing patient survival rate.

Conflict of interest:

The authors declare that they have no conflict of interest.

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