

Clinical Signs of Paraquat Poisoning in Patients Admitted to the Poisoning Section 2009-2015, In Razi Hospital (Ahvaz): A Review of 207 Cases

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ABSTRACT

Introduction: Paraquat (PQ), a toxic herbicide, is characterized by multi-organ failure, which can induce significant mortality and morbidity. In this research, the factors related to PQ poisoning have been investigated in the Ahvaz Province of Iran.

Methods: Demographic and clinical presentation data were collected and evaluated in individuals referred to the poisoning section of Razi Hospital, Iran, 2009–2015. In order to assess factors related to PQ poisoning, an individual questionnaire was developed. Physicians treated two hundred seven patients (61.35% men and 38.65% women) with PQ poisoning. All patients received vitamin C (3 g/day), vitamin E (200-4000 mg/day), NAC (20 mg/kg IV infusion stat then 50 mg/kg q12), and pulse therapy. Activated Charcoal (AC) and dialysis applied for 62.31% and 22.22% of patients, respectively.

Results: The mean age of cases was 24.06 ± 8.31 years, and the majority of them (43.20%) were 10-20 years of age. The most common on-admission clinical findings of the patients (63.28%) were nausea, vomiting, and pain. The rate of suicide was 91.78%, and the overall mortality rate was 17.87%. Death was significantly higher in patients with respiratory distress (12.56%, $P < 0.001$), renal dysfunction (9.66%, $P < 0.001$), and hepatic dysfunction (7.24%, $P < 0.002$). In patients who received intubation, pulse therapy, dialysis, AC, and NAC, 85%, 82.12%, 52.17%, 89.92%, and 83.09% of the cases have been recovered and discharged from hospital, respectively.

Conclusion: Knowing about the clinical presentation, evaluation, and treatment options for PQ poisoning is essential to reduce morbidity and mortality in these cases. The main way to manage PQ poisoning, as in the past, mainly has supportive care.

Keywords: Clinical Signs; Paraquat; NAC; Ahvaz Razi Hospital

INTRODUCTION

Paraquat (1,1'-dimethyl-4,4'-bipyridylium dichloride, PQ), also known by the brand name of gramoxone, is a member of the bipyridyl herbicide family, discovered in 1955 and developed in early 1960. PQ is produced by many factories and is very widely used to control grasses and weeds in both agricultural and nonagricultural all over the world. It is commercially available in 20% concentrated, 2.5% granules, and 0.2% aerosol formats. PQ is highly toxic and can cause fatal poisoning when ingested or inhaled. Poisoning by PQ is a major medical problem in parts of Asia, while sporadic cases occur elsewhere [1-4]. Self-poisoning with pesticides is a major public health problem in developing countries, with an estimated 300,000 deaths occurring in the Asia-Pacific region yearly [2].

PQ has a violent effect on the lungs and may damage other important organs such as the kidneys, liver, heart, adrenal glands, central nervous system, muscles, and spleen. Ultimately, it causes multiple organ dysfunction. The mechanism of PQ toxicity is not completely known, but in previous studies, it was shown that the lungs are the primary target of PQ toxicity, which is affected by all routes of administration. The molecular mechanisms underlying PQ poisoning can be regarded as follows; it can cause interference with oxidation and reduction, redox cycle, and can lead to depletion of cellular NADPH, which can consequently result in the production of free radicals like oxygen and nitrogen species, and then in damage to macromolecules such as lipids, proteins, and DNA [5,6]. PQ toxicity in the lungs can induce inflammation,

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with leukocyte recruitment and late pulmonary fibrosis, leading to hypoxemia unresponsive to treatment. Clinical manifestations of PQ poisoning are categorized into mild (less than 20 mg PQ ion/kg), severe (20–40 mg PQ ion/kg), and fulminant stages (> 40 mg PQ ion/kg), based on the exposure dose [7-9]. Pesticide poisoning comprises 2%-3% of reported poisoning cases to Iranian Drug and Poison Information Centers. This study aims to analyze statistical data to reduce the complications and adverse outcomes in this area and provide PQ poisoning solutions.

MATERIALS AND METHODS

In this cross-sectional study, demographics and clinical presentation data were collected and evaluated in individuals referred to the poisoning section of Razi Hospital, Iran, 2009-2015. In order to assess factors related to PQ poisoning, individual questionnaires were developed. In this study, two hundred seven patients (61.35% men and 38.65% women) with PQ poisoning were reviewed. All patients received vitamin C (3 g/day for five days), vitamin E (200-4000 mg/day), NAC (20 mg/kg IV infusion stat then 50 mg/kg q12 for three days), and pulse therapy. Activated charcoal (AC) and dialysis applied for 62.31% and 22.22% of patients, respectively. In this study, we used a demographic information checklist including age, sex, degree of education, time of the poisoning, job of patients, manner of poisoning, cause of poisoning, initial tests of patients at the time of the visit, initial symptoms of patients and duration time between poisoning and referral to the hospital. Data are presented in numbers and percentages for qualitative values, in means, standard deviations, and medians for quantitative values. Data are analyzed using the Statistical Package for the Social Sciences (SPSS) version 22.0 (SPSS Inc., Chicago, IL, USA). For outcome analysis, the level of significance was set at $P < 0.05$.

RESULTS

Sociodemographic profile and circumstances of poisoning during the study period, 207 patients (61.35% men and 38.65% women) with PQ poisoning were treated at Razi Hospital. The majority of the patients (43.48%) were aged 10 to 20 years. Approximately sixty-three percent of patients (132 patients) were unmarried, and the rate of suicide was 91.78% (190 patients). The majority of patients (89.85%) arrived at the hospital within less than 20 hours of poison ingestion.

Clinical findings and treatments

Renal dysfunction (75.84%), vomiting, nausea and pain (63.28%), pulmonary dysfunction (62.80%), and liver dysfunction (31.40%) were the most prevalent on-admission clinical outcomes of the patients treated at Razi Hospital (Figure 1). The main way to manage PQ poisoning, as in the past, is mainly supportive care.

One hundred twenty-nine of the patients (62.31%) were given activated charcoal. Forced gastric lavage was not performed in higher-risk patients with perforation, in the presence of corrosive mucosal damage. Fluid and electrolyte were administered to all patients to replace gastrointestinal (GI) losses, and antioxidants, including N-acetylcysteine (100 mg/kg IV stat), vitamin E (100 IU daily IV), and C (500 mg daily IV), were applied to all patients to improve the toxic effects of PQ. Pantoprazole (40 mg twice daily) was given to all patients, and higher doses of pantoprazole (8 mg/hour) were administered to patients with upper GI bleeding and GI irritation to reduce the complications of caustic GI mucosal

injuries.

Pulse therapy with methylprednisolone (1 g daily for three days) and cyclophosphamide (15 mg/kg daily for two days) was applied for all patients to reduce the PQ-induced progressive systemic damages. For removal of the poison from the blood circulation, 46 patients (22.22%), including twenty-two who later died, underwent hemodialysis. The majority of patients (187 patients, 90.33%) required ICU admission (Figure 2).

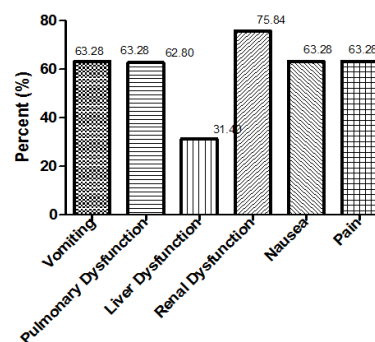


Figure 1: On-admission clinical findings of the patients (n=207).

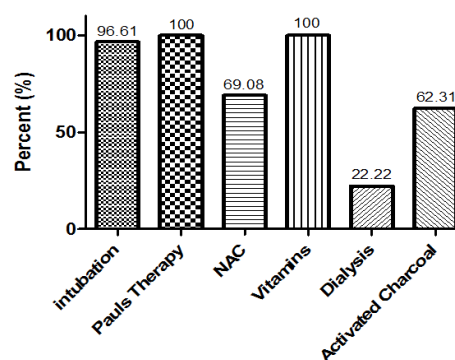


Figure 2: Therapeutic action.

Outcomes and prognosis analysis

Twenty-two patients died as a result of complications. Variables with acceptable frequency ($n > 10$) for statistical analysis were compared between death and survival outcomes to assess the impact of clinical findings and circumstances of poisoning on PQ poisoned patients' outcomes. In patients with liver dysfunction (23.07 vs. 62.93%, $P < 0.002$), renal dysfunction (12.73 vs. 87.27%, $P < 0.001$), and pulmonary dysfunction (12.56 vs. 87.44%, $P < 0.001$) rate of death was significantly higher compared to another patient. Furthermore, in this study the relationship between survival status and factors associated with treatment outcome such as pulse therapy (18 vs. 82%, $P = 0.008$), dialysis (47.83 vs. 52.17%, $P < 0.001$), active charcoal (10.08 vs. 89.92%, $P < 0.001$), and intubation (14.49 vs. 85.51%, $P < 0.001$) were assessed, and it was shown that the patients recovered and discharged from hospital (Table 2).

DISCUSSION

BPQ poisoning is rare, but with high potentially fatal. Specific antidote or treatment and generally accepted guidelines are not known for PQ poisoning. In this regard, for PQ poisoning, knowing about the clinical presentation, evaluation, and treatment options are essential to average mortality and morbidity in these cases. The mean age of poisoned persons in this study was 24.06 ± 8.31 years,

which agreed with the findings of Mohamad et al. [9]; However, the mean age of poisoned persons in studies of Weng et al., [10] Wu et al., [11] and Gil et al., [12] were not in line with the findings of our study, the reason for such a difference can be the differences between statistical society. The findings in this study showed that nausea, vomiting, pain, and respiratory failure were the most important poisoning reported signs, according to Rahmani et al. [3]. A study performed by Wu et al. [11] also reported respiratory arrest and renal impairment. However, those results were not consistent with the present study's findings; this may be a result of differences in the amount of poison, age of the patients, and referral method of the Razi Hospital. According to these findings, 37 patients (17.87%) died; this finding is in line with the results of a study by CAI et al. [12]. Unlikely, these findings are not consistent with the results of Rahmani et al., [3] Tan et al., [13] Weng et al., [10] and Wu et al., [11]. The disparity in the study duration, amount of patients, types of treatments, types of medications used, examination facilities, the indication of admission, and the modification of the therapeutic methods could be the major reasons for this difference. Our study's rate of suicide was 91.78%, which is consistent with the results of Rahmani et al. [14]. On the other hand, the rate of suicide reported by Gil et al. [12] was different from the present study results, which can be due to cultural differences in societies. In this study, 62.80% of poisoned people suffered from lung injuries that are consistent with the findings of Goudarzi et al. [15] and inconsistent with the study of Lin et al. [16] and Rahmani et al. [3]. In the current study, 75.84% of patients had kidney injuries; this finding is not in line with the study results by Rahmani et al. [3]. The difference in PQ consumption and the difference in treatment methods are reasons for this disparity. The findings in this study showed that 42.59 percent of exposed patients needed to be intubated, closed with the finding of Samimi et al. [17]. However, intubation in the study of Zawahir et al. [18] was not prescribed for any of the patients, which is not in line with our study's findings; the difference in therapeutic indications can explain the reason for this difference. The percent of pulse therapy prescribed in the study of Lin et al. was similar to our findings [16]. On the other hand, Wu et al. [11] reported that 61.1% and 52.9% of their patients cleared and died after pulse therapy prescribed, respectively, which does not follow the findings of the present study. One of the possible reasons is the difference between the amount of poison and the difference in treatment methods. According to the findings, prescribed activated charcoal for 63.33% of the patients is consistent with the results of Rahmani et al., [3] and Wu et al., [11]. In this study, 139 (67.14%) patients were admitted from 1 to 5 days, which is consistent with the findings of Weng et al. [10]. However, the findings of several studies, like Wu et al., [11] and Tan et al., [13] showed the mean duration of admission, which is not in agreement with the findings of the present study; the reasons for noncompliance of the two above studies are the difference in the amount of poisoned, time of referral, location of the patients, age, and gender. Also, in this study, a significant relationship between the amount of poison and viability was reported, which in the context of this finding, consumption of 100-500 cc of the PQ had the highest (26.29%) rate of mortality (Sig. 0.02). Findings of Goudarzi et al. [15] confirmed the result of present research. In the present study, there was no significant relationship between poison consumption and mortality (Sig 0.078), that is consistent with the study of Tan et al. [13]. Whereas, Goudarzi et al. [15] found a significant relationship between poisoning and death, in patients with PQ poisoning, which is not consistent with the findings of the present study; it

was concluded the reasons for this discrepancy were the difference in the amount of PQ consumption, age, gender, and treatment options. There was a significant relationship between death and pulmonary dysfunction in the present study (Sig 0.03), agreed with this finding, Kanchan et al., [19] Afzali et al., [20] and Wu et al., [11] found that there is a significant relationship between pulmonary dysfunction and death. In this study, we showed that significant relationship between PQ consumption and hospitalization in ICU (Sig. 0.034), this finding is consistent with the results of Rahmani et al., [14] and Samimi et al. [17]. There was a significant relationship between mortality and liver dysfunction, which is consistent with the findings of Kanchan et al. [19]. Nevertheless, due to the small population of patients and involved a short period of follow-up, more studies is needed to confirm our results.

CONCLUSION

It can be concluded that the highest prevalence of PQ poisoning (91.70 percent) among patients, affecting young people in the age group of 10-30 years. Therefore, preparing and developing a comprehensive and continuous training program to increase awareness among family and community level are needed. It is hoped that by reducing financial and psychological pressures and reforming the rules and regulations, more difficult access to PQ will decrease suicide rates in this group. Knowing about the clinical presentation, evaluation, and treatment options for PQ poisoning is important to reduce morbidity and mortality in these cases.

LIMITATION

Serum levels of PQ were not measured in the majority of PQ poisoned patients; meanwhile, the diagnosis in our study was based on the patient's history and clinical examination.

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CONFLICT OF INTEREST

It can be concluded that the highest prevalence of PQ poisoning (91.70 percent) among patients.

REFERENCES

1. PAN. Adverse health effects caused by paraquat. Public Eye; Pestic Action Netw UK Pestic Action Netw Asia-Pacific. Pesticide Action Network.2017;1:1-88
2. Manuel C, Gunnell DJ, Van Der Hoek W, Dawson A, Wijeratne IK, Konradsen F. Self-poisoning in rural Sri Lanka: Small-area variations in incidence. BMC Public Health.2008;8:1-8.
3. Rahmani A, Forouzandeh H, Khatibi MT. Medical management and outcome of paraquat poisoning in Ahvaz, Iran: A hospital-based study. Asia Pacific J Med Toxicol.2015;4(2):74-78.
4. Sabzghabae AM, Eizadi-Mood N, Montazeri K, Yaraghi A, Golabi M. Fatality in paraquat poisoning. Singapore Med J.2010;51(6):496-500.
5. Blanco-Ayala T, Andérica-Romero AC, Pedraza-Chaverri J. New insights into antioxidant strategies against paraquat toxicity. Free

- Radic Res.2014;48(6):623-640.
6. Ranjbar A. Evidence of Oxidative Damage in Paraquat Toxicity. Zahedan J Res Med Sci J homepage.2014;16(12):1-7.
 7. Weng CH, Chen HH, Hu CC, Huang WH, Hsu CW, Fu JF, et al. Predictors of acute kidney injury after paraquat intoxication. Oncotarget.2017;8(31):51345-51354.
 8. Jones AL, Elton R, Flanagan R. Multiple logistic regression analysis of plasma paraquat concentrations as a predictor of outcome in 375 cases of paraquat poisoning. QJM - Mon J Assoc Physicians.1999;92(10):573-578.
 9. Mohamed F, Endre Z, Jayamanne S, Pianta T, Peake P, Palangasinghe C, et al. Mechanisms underlying early rapid increases in creatinine in paraquat poisoning. PLoS One.2015;10(3):1-16.
 10. Weng CH, Hu CC, Lin JL, Lin-Tan DT, Hsu CW, Yen TH. Predictors of acute respiratory distress syndrome in patients with paraquat intoxication. PLoS One.2013;8(12):1-8.
 11. Wu WP, Lai MN, Lin CH, Li YF, Lin CY, Wu MJ. Addition of immunosuppressive treatment to hemoperfusion is associated with improved survival after paraquat poisoning: A nationwide study. PLoS One.2014;9(1):e87568.
 12. Cai, Quan and Liu Z. An analysis of relevant factors of early death in acute paraquat poisoning. Chin Critic Care Med.2014;26(6):379-382.
 13. Chia BH, Chia A, Ng WY, Tai BC. Suicide methods in singapore (2000-2004): Types and associations. Suicide Life Threat Behav.2011;41(5): 574-583.
 14. Rahmani AH, Jafari M, Farnam M, Zafari J. Evaluation Of Epidemiologic Of Drug Poisoning In The Ahvaz Razi Hospital In The Years Of 2004-2008. J Forensic Med.2015;21(73):43-46.
 15. Goudarzi F, Armandeh J, Jamali K, Rahmati H, Meisami A. Mortality Analysis of Patients with Paraquat Poisoning Treated at Two University Hospitals in Shiraz , Iran.2014;3(4):141-145.
 16. Lin J, Chen K. Improved survival in severe paraquat poisoning with repeated pulse therapy of cyclophosphamide and steroids. Intensive Care Med.2011;37(6):1006-10013.
 17. Samimi A, Rahmani ALIH, Ababaf R, Zeidooni L. An Investigation of Clinical Symptoms and Treatment of Organophosphate Poisoning among Patients Referred to Razi Hospital during 2006 - 2012. Asia Pac J Med Toxicol.2016;5(4):107-110.
 18. Zawahir S, Roberts DM, Palangasinghe C. Europe PMC Funders Group Acute intentional self-poisoning with a herbicide product containing fenoxaprop-P-ethyl, ethoxysulfuron and isoxadifen ethyl . A prospective observational study. Clin Toxicol Phila.2011;47(8):792-797.
 19. Kanchan T, Bakkannavar SM, Acharya PR. Paraquat Poisoning: Analysis of an Uncommon Cause of Fatal Poisoning from Manipal, South India. Toxicol Int.2015;22(1):30-34.
 20. Afzali S, Rashidi P. A one-year study of mortality due to drug and chemical poisoning in sina hospital of hamadan. Avicenna J Clin Med.2003;10(3):62-66.