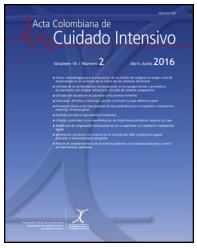
Acta Colombiana de Cuidado Intensivo xxx (xxxx) xxx–xxx

Asociación Colombiana de Medicina Crítica y Cuidado Intensivo

Acta Colombiana de Cuidado Intensivo

www.elsevier.es/acci



CASE REPORT

Paraquat fulminant poisoning: Case report

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Received 19 May 2023; accepted 31 August 2023

KEYWORDS
Paraquat intoxication;
Self-poisoning;
Suicide attempt;
Pesticides;
Case report

Abstract Paraquat is one of the most widely used non-selective herbicides in the world, however, it is prohibited in many countries due to its high toxicity and mortality rate. Herein, we present a case of fulminant PQ poisoning in a 21 years-old woman with a six weeks pregnancy, and a history of sexual abuse and rape; computed tomography showed disseminated micronodular alveolar infiltrates and septal thickening. It rapidly progressed to severe acute respiratory distress syndrome, requiring endotracheal intubation; however, paraquat is known to generate reactive oxygen species that cause cell damage through lipid peroxidation, mitochondrial activation, and apoptosis following oxygen exposure. Therefore, in these cases, the line between the risk and benefit of oxygen therapy is very thin. Despite receiving timely treatment, the serious hemodynamic and respiratory deterioration evolved into multiple organ failure and later the death of the patient. Paraquat poisoning severe intoxication has a dim prognosis, although early diagnosis results in therapeutic challenge due to severe respiratory compromise. We also present a brief review of the literature, as well as a discussion of the treatment for paraquat fulminant poisoning.

PALABRAS CLAVE
Intoxicación por paraquat;
Auto-envenenamiento;
Intento de suicidio;
Pesticidas;
Informe de caso

Intoxicación fulminante por paraquat: reporte de caso

Resumen El paraquat es uno de los herbicidas no selectivos más utilizados en el mundo, sin embargo, está prohibido en muchos países debido a su alta toxicidad y tasa de mortalidad. El envenenamiento por paraquat (PQ por sus siglas en inglés) por lo general resulta de una exposición suicida, ocupacional o accidental. Presentamos un caso de intoxicación fulminante por PQ en una mujer de 21 años con un embarazo de seis semanas y antecedentes de abuso sexual y violación; La tomografía computarizada mostró infiltrados alveolares micronodulares

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https://doi.org/10.1016/j.acci.2023.08.006

Please cite this article as: M.A. Amezcua-Gutiérrez, J.A. Castañón-González, N.I. Medveczky-Ordóñez et al., Paraquat fulminant poisoning: Case report, Acta Colombiana de Cuidado Intensivo, https://doi.org/10.1016/j.acci.2023.08.006

diseminados y engrosamiento septal. Evolucionó rápidamente a síndrome de distrés respiratorio agudo severo, ameritando intubación endotraqueal, sin embargo, se sabe que el paraquat genera especies reactivas de oxígeno que producen daño celular a través de la peroxidación de lípidos, activación mitocondrial y apoptosis posterior a la exposición con oxígeno, por lo que en estos casos es muy delgada la línea entre el riesgo y beneficio de la oxigenoterapia. A pesar de recibir tratamiento oportuno, el grave deterioro hemodinámico y respiratorio evolucionó a falla multiorgánica y posteriormente al fallecimiento del paciente. La intoxicación grave por paraquat tiene un pronóstico sombrío, aunque el diagnóstico temprano da como resultado un desafío terapéutico debido al compromiso respiratorio grave. Se presenta una breve revisión de la literatura, así como una discusión sobre el tratamiento de la intoxicación por paraquat fulminante.

Introduction

Pesticide poisoning accounts for about one-third of the world's suicides. According to the World Health Organization pesticide toxicity classification, toxicity depends on their lethal dose 50 (LD50): Class IA extremely hazardous (<20 mg/kg), class IB highly hazardous (20–200 mg/kg), class II moderately hazardous (200–2000 mg/kg) and class III slightly hazardous (>2000 mg/kg).[1]

Since its introduction in agriculture in 1962, paraquat (1,1′-dimethyl-4,4′-bipyridinium dichloride; PQ) is one of the most widely used non-selective herbicides in the world. Despite its ban in the European Union since 2007, – due to its high toxicity and associated mortality rate –, it stills in use in the United States of America and Latin America.[2]

After ingestion, the gastrointestinal tract absorbs < 20%, and approximately 90% of absorbed PQ is excreted unchanged by the kidneys. Because it's not actively metabolized in the body, PQ distributes to highly perfused organs such as lungs, kidneys, liver, and muscles, remaining partially in the intravascular space.[3] Kidneys exposed to PQ develop large vacuoles in the proximal convoluted tubules, leading to necrosis and decline in renal function with subsequent increase in plasma concentrations; which further contributes to its toxicity. Lung toxicity generates pulmonary edema, hypoxia, respiratory failure, and pulmonary fibrosis.[4]

Clinical report

Herein, we present a case of fulminant PQ poisoning in a 21 years-old nurse student with a six weeks pregnancy, and a history of sexual abuse and rape; no pathological history of importance for his current condition. She was admitted to the Emergency Room of a local hospital with vomit, malaise and abdominal pain, 20 min after 100 mL (20 g active ingredient) of 25% paraquat dichloride ingested in a suicide attempt. She received immediate treatment with activated charcoal after gastric lavage, and was admitted for supportive care. Six days later she was transferred to our ICU with acute kidney injury (AKI) and acute liver failure. On admission, she had jaundice and was tachypneic, with a sore throat and tongue, SpO_2 was 70% on room air (recovering to 90% with oxygen supplementation); bilateral subscapular rales. No neurological deficit was noted. Laboratory tests reported a serum creatinine of 3.4 mg/dL, total bilirubin 5.8 mg/dL and elevated aminotransferases (AST 300 UI/L, ALT 382 UI/L). Arterial blood gas analysis at an FiO_2 60% pH 7.45, PaO_2 59 mmHg, $PaCO_2$ 32 mmHg, PaO_2/FiO_2 ratio 98 mmHg and plasma bicarbonate concentration 16.5 mmol/L. Transvaginal Ultrasound showed intrauterine singleton pregnancy without embryonic pole or yolk sac. Chest X-ray and single phase chest computed tomography showed disseminated micronodular alveolar infiltrates and septal thickening (Fig. 1).

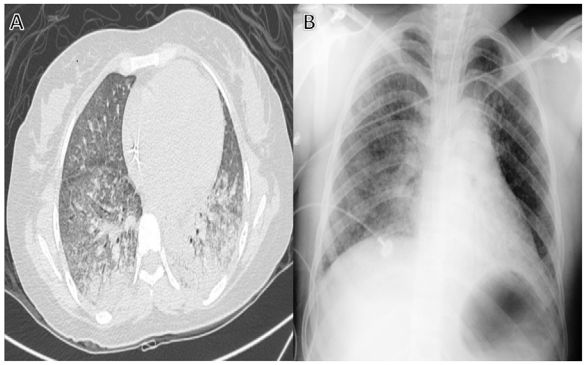

Figure 1 Chest computed tomography single phase and plain chest X-ray on post-ingestion days 7 (A) and 11 (B) respectively. Showed multiple micronodular and alveolar infiltrates disseminated of predominance toward the posterior regions of the basal lobes and bilaterally with areas of septal thickening.

Antioxidative and antinflammatory therapy – with acetylcysteine (20 g in a 24 h IV infusion drip) and boluses of methylprednisolone were administered in an attempt to reduce reactive oxygen species formation. On second day of ICU stay (post-ingestion day 8). She was intubated and mechanical ventilation started. On the fourth day (post-ingestion day 10), (Fig. 2) despite maintaining optimal PEEP and lung protection strategy, hipoxemia persisted, therefore

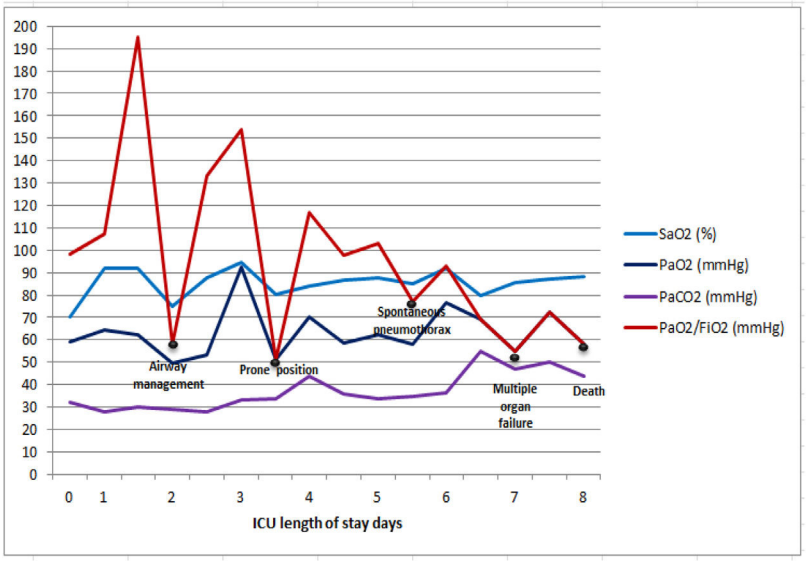

Figure 2 Pulmonary gas exchange parameters evolution.

prone position ventilation and vasopressors were started, which resulted in mild respiratory improvement. Renal function also improved. On sixth day (post-ingestion day 12), a left pneumothorax was noted and a thoracostomy tube was placed. On the seventh day (post-ingestion day 13), hemodynamic and respiratory deterioration persisted, with coagulopathy requiring high ventilatory parameters, vasopressors, and transfusion of packed red cells and plasma. After a protracted clinical course she died with multiple organ failure on day 14 after PQ ingestion.

Discussion

From all pesticides, PQ intoxication accounts for the highest mortality. Clinical features of acute PQ intoxication can be classified into three categories: (1) Mild poisoning (<20 mg/kg of 20% PQ), in which patients have minor gastrointestinal symptoms and a full recovery; (2) Severe poisoning (20–40 mg/kg of 20% PQ) were patients develop sore tongue, shortness of breath, agitation, abdominal discomfort, head lightness, tachypnea, tachycardia, AKI, and acute lung injury with progressive pulmonary fibrosis. Death occurs 2–3 weeks after a protracted clinical curse, as result of respiratory failure; and (3) Fulminant poisoning (>40 mg/kg of 20% PQ) with multiple organ failure leading to death within hours to few days after ingestion.[2,5] Several pathways underlie the critical toxicity of PQ, such as its elevated concentration reached in lungs due to its high affinity for alveolar cells, which form reactive oxygen species that cause cellular damage via lipid peroxidation, activation and release of NF-$\kappa\beta$, tumor necrosis factor-α, interleukin (IL) 1 and IL-6, transforming growth factor (TGF)-β1, that produce mitochondrial damage and apoptosis. PQ-induced lung injury has two phases: characterized by an early destruction of alveolar epithelial cells and a proliferative period with infiltration of inflammatory cells, alveolitis, edema, and finally pulmonary fibrosis.[6,7]

The diagnosis of PQ poisoning is easy with an accurate history of exposure, physical exam – like in this case – and the specific laboratory tests of urine sodium dithionite screening test. Supportive treatment should be initiated without delay, because there is not a specific antidote. Initial management focuses on prevention of further absorption and gastrointestinal decontamination that should be performed immediately, within two hours post-ingestion. Oxygen supplementation should be avoided – if possible –, unless PaO_2 is less than 60 mmHg, because it can potentiate paraquat-induced lung injury. Trying to avoid free radical injury to the lungs, vitamins C and E, N-acetylcysteine, desferrioxamine, nitrous oxide, corticosteroids, and cyclophosphamide have not been effective to prevent pulmonary fibrosis.[8,9] Paraquat elimination from the circulation through hemoperfusion or hemodialysis is of some benefit when instituted early and in those cases with ''borderline exposure'' already with AKI and without pneumonitis, but it is useless in severe intoxication or when it is indicated late.[7]

The prognosis of paraquat poisoning is related to two main factors: plasma PQ concentration and time elapsed since ingestion, which was very long in this patient. Although PQ severe intoxication has a dim prognosis, early diagnosis and aggressive management of paraquat poisoning can reduces mortality.[10] It is important to consider the PQ intoxication cause in this patient, since the history of sexual abuse and rape are strongly associated with suicide attempts and consequently represent a health problem that should be taken care of immediately.

Conflict of interests

The authors declare that they have no conflict of interest.

Acknowledgements

The authors would like to thank Hospital Juárez de México for the facilities that it provided to conduct this article.

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