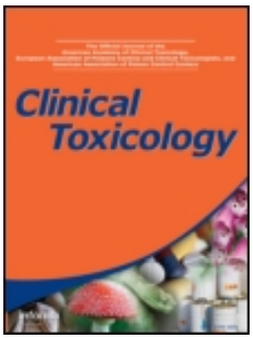

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LETTER TO THE EDITOR

Human poisoning with prochloraz imidazole fungicide

To the Editor:

Prochloraz (*N*-propyl-*N*-[2-(2,4,6-trichlorophenoxy)ethyl]-1*H*-imidazole-1-carboxamide) is a broad-spectrum imidazole fungicide.[1] There are very few data relating to adverse effects in humans from acute exposure to prochloraz. In 2012, Gil et al.[2] described a case of acute prochloraz–manganese complex intoxication which was successfully treated with extracorporeal elimination. The manganese levels on the first, second, and fourth hospital days were 34.1, 23.6, and 12.5 μg/l, respectively.[2] The case is interesting in terms of the acute toxicity of prochloraz relative to the amount ingested (12 g, LD50 1200 mg/kg), but it is not unreasonable to believe that prochloraz was responsible and that there is little else but inert clay in the solid formulations. The "success" of dialysis in that case was a drop in serum manganese levels but it is not clear whether: 1) removal was due to dialysis – although not implausible, 2) the levels were toxic given the low toxicity of soluble manganese compounds, and 3) the dialysis had any clinical impact. In this article, we report a suicide case of acute pure prochloraz poisoning, which was complicated by severe bradycardia, shock, and metabolic acidosis.

A 31-year-old depressed Filipino maid was admitted to the hospital following ingestion of 10 ml prochloraz 25% emulsifiable concentrate (2.5 g, Tai Yeh, Taiwan). The symptoms of prochloraz toxicity developed quickly with salivation and oral pain, followed by nausea, vomiting, and abdominal discomfort. The patient was brought to our hospital in an hour. On admission she was confused with a Glasgow Coma Scale of 12 (E3V3M6), heart rate was 55 beats per minute, and blood pressure was 82/55 mmHg. An arterial blood gas test showed metabolic acidosis with partial respiratory compensation (pH 7.326, carbon dioxide 27.8 mmhg, oxygen 72.7 mmhg, bicarbonate 14.2 mEq/L, base excess – 11.8 mmol/L, oxygen saturation 93.9%). Electrocardiogram showed sinus bradycardia. Echocardiography revealed adequate ventricular contractility with a small amount of pericardial effusion (< 100 ml). Hemodynamic stability was regained after fluid challenge and inotropic agent infusion. Detoxification protocol was performed with gastric lavage (1.5 h after ingestion), followed by activated charcoal infusion. Endoscopy examination disclosed Grade 2a corrosive esophageal injury. The following course was uneventful, and she gradually improved and was discharged in 9 days.

The data indicate that prochloraz was very toxic, causing not only esophageal corrosion, but also bradycardia, shock, and metabolic acidosis. There is no antidote for prochloraz intoxication. Gastric lavage and active charcoal infusion were performed even though the time elapsed was slightly longer and the patient was mildly confused.

The hazards of chronic low dose prochloraz exposure to human beings have been characterized.[3] In terms of acute toxicity, an acute reference dose of 0.1 mg/kg bw was established, which is based on a no-observable-effect level of 10 mg/kg bw per day for effects on the liver at day 3 in a 14-day study in dogs, and a safety factor of 100.[3] Therefore, this limit has been exceeded after ingestion of 10 ml prochloraz 25% emulsifiable concentrate. Nevertheless, it should be mentioned that levels in excess of the regulatory acute reference dose do not likely indicate human acute toxicity.

Conversely, the mechanism of prochloraz-induced cardiotoxicity remains unclear. Domingues et al. reported that the acute toxicity of prochloraz for zebrafish early life stage and adult stage was similar with 96-h lethal concentration-50 values of 8.5 and 4.6 mg/L, respectively.[4] Furthermore, the prochloraz might be teratogenic and could induce many embryonic developmental anomalies, for example spine deformations, edemas, lack of pigmentation, slower heart rate, and complete hatching failure.[4] The teratogenicity and developmental studies in fish are not readily extrapolatable to humans.

Finally, other potential contributors to the toxicities in this patient are formulation composition. This product is 25% prochloraz, but the remaining 75% is split between an organic solvent (petroleum thinner-170), stabilizer, and emulsifier. The petroleum thinner contains 98% aromatics and 1% xylene. The 1% xylene is highly unlikely to account for toxicity, as this would be about 80 mg of xylene – but this solvent is a variant of heavy aromatic naphtha and is a mixture of xylene, cumene, toluene, and bi-cyclic like naphthalene which collectively could contribute significantly to brain toxicity. Therefore, what we have learned from this case is either there is another component of the formulation which has substantial toxicity, or that prochloraz has greater human toxicity than anticipated on the basis of animal data. The previously reported case involving prochloraz as a dry component on a clay matrix suggests the latter. In either event, clinicians should be aware that ingestion of this formulated material appears to cause serious toxicity even with levels of intake below those causing serious toxicity in animals and should be prepared to observe the patient and provide aggressive support if needed.

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Declaration of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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