Fungicide (Rubigan®) Overdose Mimicking Organophosphate Poisoning

Shaden Salameh MD[1,2], Teddy Weiss MD[1] and Yona Amitai MD MPH[3]

Departments of [1]Internal Medicine and [2]Emergency Medicine, Hadassah-Hebrew University Medical Center (Mount Scopus Campus), Jerusalem, Israel
[3]Public Health Service, Ministry of Health, Jerusalem, Israel

Key words: Rubigan®, fungicide, poisoning, organophosphate

IMAJ 2008;10:804–805

Severe poisoning from organophosphate or carbamate insecticides is common and widely recognized. The toxidrome includes hypersecretion syndrome, manifested as salivation, lacrimation, diarrhea, bronchorrhea, as well as bronchoconstriction, bradycardia, depression of the central nervous system, miosis, fasciculations, muscle weakness and seizures. The classical clinical appearance facilitates a prompt diagnosis. The diagnosis is confirmed by decreased serum acetylcholine esterase activity [1,2].

We present a case of intoxication with fenarimol and triadimenol, the active ingredients of the fungicide Rubigan® that evoke clinical signs and symptoms which can be confused with organophosphate toxidrome. Our patient had severe intoxication but recovered uneventfully with supportive treatment. To the best of our knowledge there is only one report of near fatal intoxication by Rubigan and no reports of severe toxicity with recovery [3].

Fenarimol is a pyrimidin-5-yalbenzhydrol fungicide and a steroid demethylation inhibitor [4]. Triadimenol is a conazole fungicide and steroid demethylation inhibitor as well [4]. These substances are usually used to treat seeds with mold and their usage is quite widespread in agriculture. Recognition of the potential danger of these compounds is important for a prompt diagnosis and treatment, as well as for primary prevention by means of increased awareness and appropriate product labeling.

Patient Description

A 65 year old man was brought unconscious to the emergency department by his family. He exhibited lacrimation, salivation and shortness of breath shortly after an intentional ingestion of a white liquid. He was a non-smoker with a history of diabetes, hypertension and ischemic heart disease, and prior to his admission was stable and well controlled with aspirin and an angiotensin-converting enzyme inhibitor.

Shortly before his admission, he ingested approximately 300 ml of a white liquid material with a strong aromatic odor, found in his garden and brought to the hospital later. Upon admission he was unconscious with labored breathing. His blood pressure was 100/60 mmHg, heart rate 56 beats/minute regular, respiratory rate 10 breaths/min. He was afebrile and pulse oxymetry was 87% on room air. On physical examination he was barely responsive to deep pain and his Glasgow Coma Scale score was 8. His pupils were equal but constricted with a minimal response to light. Lacrimation and salivation were noted. Pulmonary examination revealed bilateral ronchi. The rest of the physical examination was unremarkable and he did not have seizures.

Laboratory tests – including electrolytes, kidney and liver function tests, sedimentation rate, coagulation tests and cardiac enzymes – were within normal limits, apart from hypokalemia (2.7 mmol/L) and leukocytosis (14,000 cells/mm^3) with normal neutrophil count (41%). His electrocardiogram was normal, except for sinus bradycardia and a right bundle branch block, known prior to his admission. His chest X-ray revealed bilateral interstitial markings and his echocardiography was normal. Urine toxic screen was negative for barbiturates, benzodiazepines, opiates, methadone, amphetamines, cocaine and cannabinoids. Blood, sputum, stool and urine cultures were sterile.

In the emergency department he underwent primary stabilization that included intubation and mechanical ventilation, intravenous fluid resuscitation, bronchodilators by inhalations and IV atropine for symptomatic bradycardia; activated charcoal was given through nasogastric tube. At this point the liquid material was brought and identified by a family member; the name "Rubigan" appeared on the label. A toxicological consultation recommended mainly supportive treatment and withholding the use of toxogonin since the material had been identified and the acetylcholine esterase level was normal (6 units/ml) at admission (normal range 3–9 units/ml).

The patient was admitted to the intensive care unit and the conservative therapy was continued. Organophosphate poisoning was still suspected; however, his serum acetylcholine esterase levels were normal in two consecutive samples taken during the first 12 hours of his admission. The patient gradually regained consciousness, the antibiotics were discontinued and he was extubated. There were no further hypersecretions and the heart rate was normal. Two days after admission he recovered uneventfully and was discharged without neurological deficit.

Upon investigation, the ingested fluid was found to be Rubigan. A gas chromatography-mass spectrophotometry performed by the forensic laboratory of the Israel Police identified the active ingredients as fenarimol and triadimenol – fungicides used in agriculture.

After discharge, the patient was treated in a psychiatric clinic with antidepressants and no further suicide attempts were made. Follow-up of 2 years showed no impairment in cognition or other long-term sequelae.

Discussion

We present a case of severe acute intoxication by a fungicide containing triadimenol and fenarimol in a patient admitted to our emergency department with coma, miosis, bradycardia and hypersecretion syndrome. This clinical presentation is characteristic for organophosphate or carbamate poisoning. This suspicion was reinforced by the information about the liquid material found in his garden and apparently used for plant care that he ingested shortly before he was admitted. However, the normal serum acetylcholine esterase activity in three different samples and the identification of the material by the family and later by a special laboratory as triadimenol and fenarimol ruled out poisoning by acetylcholine esterase inhibitors.

Fungicides such as triadimenol and fenarimol are well known and are used in agriculture. Usually their usage is restricted to professional farmers and licensed exterminators to treat plants and seeds. This may explain the scarcity of reports of human poisoning.

When a patient presents with coma, miosis, lacrimation, salivation, bronchospasm and seizures after ingesting a material used in agriculture, the first tentative diagnosis is organophosphate or carbamate intoxication. This approach is important for appropriate management to achieve optimal medical outcome. It should include in addition to the supportive treatment, intravenous atropine and oximes. At the same time, it is important to keep in mind other possibilities, as in the case presented here. The implication of an accurate diagnosis of other conditions that mimic organophosphate poisoning is the withholding of oximes which are not indicated in such a case. In traidimenol and fenarimol intoxication the treatment is mainly supportive. Small doses of atropine were given to our patient as a symptomatic treatment for bradycardia, but not as a part of antidotal therapy for organophosphate poisoning, which requires higher doses and longer duration.

Our patient had a complete recovery, with no sequelae. A long-term follow-up was required because of limited experience with traidimenol and fenarimol intoxication and the possibility of delayed sequelae in organophosphate poisoning [5].

To the best of our knowledge the only previous report on Rubigan overdose was that of a patient who was found dead and the diagnosis was based on postmortem investigation, so that the clinical presentation of this intoxication could not be appreciated. The possible mechanism of poisoning is still not totally understood. The present report is the first documented overdose of Rubigan, with severe intoxication and complete recovery. Increased awareness to the toxicity of Rubigan and inclusion of an appropriate warning on the product label are required to improve its safety.

References

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Correspondence: Dr. S. Salameh, Hadassah University Medical Center (Mount Scopus Campus), Jerusalem 91240, Israel.
Phone: (972-2) 584-4111
email: shaden@hadassah.org.il