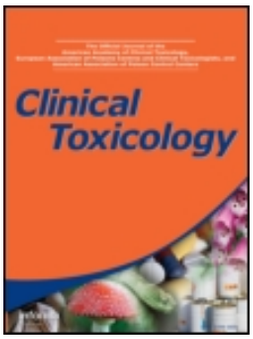

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CASE REPORT

Fatal human poisoning with Padan™: a cartap-containing pesticide

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We report a patient who ingested about 13 g of Padan SG™, a cartap-containing pesticide. After ingestion, the patient developed multiple seizures and dyspnea and lost consciousness. The patient did not recover and died on the fifth hospital day despite treatment at the early stage of poisoning. The cause of death was multisystem organ failure. Results of toxicological analysis were as follows: concentrations of nereistoxin (cartap metabolite) were 10.6 μg/mL in plasma, 18.2 μg/mL in urine, and 2.6 mg/mL in gastric fluid. Results of drug screening of urine by Triage® DOA Panels and using an organophosphate detection kit were negative.

Keywords Insecticide; Cartap; Acute fatal poisoning

Introduction

Cartap (brand name Padan) [*S*,*S*′-(2-dimethylaminotrimethylene)-bis(thiocarbamate)] is a pesticide that was first introduced in Japan in 1967 and has been commonly used to control weeds and caterpillars.[1] This pesticide was the first commercial insecticide derived from the structure of a natural toxin, nereistoxin, which is a neurotoxic substance isolated from the marine annelid *Lumbriconeresis heteropoda*. Cartap has been commonly considered to be a relatively safe compound[2] and is used worldwide.

Despite its wide usage, to our knowledge, there are few reports on human exposure to cartap resulting in clinical toxicology. Here, we report results of fatal human poisoning with cartap and its toxicity.

Case report

A 36-year-old man had a history of dysautonomia from 18 to 19 years of age but no history of attempted suicide. Following intentional ingestion of about 13 g of Padan SG™ (75% cartap), he sent an e-mail to his elder sister at about 22:00. He called an ambulance by himself at 22:34. When the ambulance arrived at 22:39 (about 40 min after his ingestion), he said he had taken the insecticide mixed in water, and he gave the container to the rescue personnel. At that time, his level of consciousness in Glasgow coma scale (GCS) was 13 (E4V4M5), his pulse rate was 130/min, the radial artery was palpable, and SpO_2 was 81% (room air). He became restless while being transported in the ambulance: his level of consciousness was GCS 9 (E4V1M4). He was supplied oxygen at 10 L/min. On arrival at the emergency room at 22:59 (about 1 h later), his level of consciousness was GCS 9 (E4V1M4), respiratory rate was 20–30/min, pulse rate was 83/min, and temperature was 36.8°C. He was intubated and mechanically ventilated for hypoxemia by shallow and decreasing spontaneous respiration at 23:20. Initial tests immediately after intubation revealed blood urea nitrogen of 9.9 mg/dL, creatinine of 0.61 mg/dL, creatinine phosphokinase (CPK) of 944 U/L, arterial pH of 6.475, $PaCO_2$ of 190.7 mmHg, PaO_2 of 74.4 mmHg (FiO_2 1.0), HCO_3 of 25.6 mEq/L, and base excess of −14.5. Tonic–clonic convulsion occurred at 23:30 and continued for several tens of seconds, so he was injected with 10 mg of midazolam. However, repeated and intermittently continued convulsion required midazolam (total 30 mg), diazepam (total 20 mg), and phenytoin (total 1,000 mg). The patient received gastric lavage at 23:55 when the convulsion decreased. At 1:35 the next day (about 3.5 hours later), a CT scan did not show any abnormality but showed brain edema 12 h after admission. A chest X-ray did not show any abnormality. Anuric acute renal failure and following high value of CPK over 10,000 IU/L occurred on the first hospital day, and DIC (platelets: 2.5×10^4/μL, PT-INR: 1.73, serum FDP: 33.1 μg/mL) developed on the second hospital day. He died from multiple organ failure on the fifth hospital day without recovery of consciousness. Autopsy was not performed.

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Toxicological analysis

Plasma, urine, and gastric fluid samples were taken during gastric lavage and the samples were stored at 4°C until analysis.

All chemicals used were of analytical reagent grade. Nereistoxin was purchased from Wako Pure Co. Ltd. (Tokyo, Japan). Cartap and its metabolite nereistoxin were determined according to Namera.[3] Briefly, benzylacetone as an internal standard and sodium hydroxide were added to a sample for hydrolysis. Cartap was converted to nereistoxin by hydrolysis.[4] Samples were extracted with cyclohexane, and the extract was concentrated to 0.1 mL and analyzed by GC–MS.

Analytical data revealed 10.6 μg/mL nereistoxin in plasma, 18.2 μg/mL in urine, and 2.6 mg/mL in gastric fluid.

Urine screening by Triage® DOA Panels for abuse drugs (Biosite Inc., San Diego, CA, USA) was negative. Urine screening using an organophosphate detection kit (Kanto Chemical Co. Inc., Tokyo, Japan) was negative. Result of drug screening in blood, urine, and stomach content by REMEDi® Drug profiling system (Bio-Rad, Hercules, CA, USA) detected an unidentified peak, which was not registered in REMEDi-HS® library.

Discussion

The toxicity of cartap has been considered to be low, and severe or fatal cases of cartap poisoning have been rare. However, it has been reported that several men died by suicide with cartap ingestion in Japan.[5,6] Cartap is obtained as a granular powder material by a brand name such as Padan. Padan contains from 2 to 75% of cartap. Four case reports on cartap poisoning, including fatal cases in two reports[7,8] and nonfatal cases in two reports,[3,9] have been published. After ingestion, the victims developed convulsion and dyspnea and lost consciousness. The clinical course of the present case was the same as those of the other four cases. The plasma concentration of nereistoxin in the present case was 10.6 μg/mL, the same as that in another fatal case reported by Bunai et al. (11.5 μg/mL).[7] On the contrary, the blood concentration of cartap was 1.14 μg/mL 3 h after ingestion in a survival case.[9] These findings indicate that the cause of death in the present case was cartap poisoning.

Cartap and its metabolite nereistoxin are thought to act by neuromuscular blockage through inhibition of the postsynaptic nicotinic acetylcholine receptor ion channel, leading to salivation, vomiting, tremor of the arms and legs and tonic or clonic convulsion, and respiratory failure and subsequent death in severe cases.[10,11] Moreover, cartap can cause Ca^{2+}-dependent contracture in both isolated mouse and rabbit phrenic nerve diaphragms, and cartap-induced reactive oxygen species (ROS) generation through a Ca^{2+}-dependent mechanism may play a central role in the myogenic contracture and myofiber injury of diaphragm leading to respiratory failure and subsequent death in rabbits.[12–14] These findings coincide with the clinical course of human acute poisoning by cartap ingestion.

Kiyota et al.[9] reported a case of cartap intoxication in a woman who ingested Padan solution containing 50% cartap. The husband discovered his wife who had vomited and lost consciousness presumably 0.45 h after ingestion. She received gastric lavage immediately after hospitalization and recovered consciousness 8 h after ingestion. Kiyota[9] recommended that gastric lavage is an effective treatment for cartap poisoning. In another case reported by Namera et al.,[3] an 83-year-old woman attempted suicide by ingestion of Padan 4R containing 4% cartap. She slipped into coma 2 h later and gastric lavage was performed 3 h after ingestion. She recovered consciousness the next day.

On the contrary, Kuwahara et al.[8] reported a fatal case of cartap intoxication in a 50-year-old female who ingested Padan containing 75% cartap. She lost consciousness and light reflex and became a cyanotic when she was discovered. Gastric lavage was performed 40 min after she had been discovered. She died from multiple organ failure with DIC on the sixth hospital day. The clinical course of that case was similar to that of our case. These findings suggested that gastric lavage was not effective in either case and that the concentration of cartap in the formula is an important factor determining prognosis, even if gastric lavage is performed at an early stage.

The mechanism of the development of brain edema in both cases was unknown, but there is the possibility that anoxia was involved.

Declaration of interest

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

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