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Case Report

Cartap poisoning: an unusual poisoning in North India

Monica Gupta*, Dipti Handa, Amit Chaturvedi, Ram Singh, S. S. Lehl

Department of General Medicine, Government Medical College and Hospital, Chandigarh, India

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***Correspondence:**
Dr. Monica Gupta,
E-mail: drmg1156@gmail.com

ABSTRACT

Cartap hydrochloride, an analogue of nereistoxin, belongs to a relatively new class of insecticidal chemistry, and its poisoning is uncommon in India. We describe a 50-year-old farmer who presented to emergency department in altered sensorium and alleged history of accidental inhalation of cartap hydrochloride while working in the fields. The patient improved with conservative management with BAL (British anti-lewisite) without any residual complications. As per the current medical literature; this is probably the first case report of cartap inhalational accidental poisoning.

Keywords: Cartap hydrochloride, Pesticide, Inhalational poisoning

INTRODUCTION

Novel plant or animal derived insecticides are in the process of development following resistance to the contemporary organochlorine and organophosphate compounds. Cartap hydrochloride is one such novel analogue of nereistoxin and is commercially known as 'padan'. It was first manufactured in Japan in 1966 and has been used in India since 1988. It was first isolated in Japan in 1967 from marine annelid Lumbrineris heteropoda.[1] It is a nereistoxin. It is commonly used in rice fields because of its paralytic toxicity against rice stem borer, *Chilo suppressalis*. Its basic chemical structure is S,S-[2-(dimethylamino)-1,3-propanediyl] dicarbamothioate (Figure 1) and is normally used as hydrochloride (cartap hydrochloride, CHC) 4% granule formulation. As per WHO, it is a moderately hazardous technical product and the maximal daily acceptable intake level is 0.05 mg/kg.[1]

The primary effect of cartap hydrochloride is through inhibition of the [^{3}H]-ryanodine binding to the Ca^{2+} release channel in the sarcoplasmic reticulum in a dose-dependent manner leading to extracellular Ca^{2+} influx and induction of internal Ca^{2+} release.[2] This results in tonic diaphragmatic contraction which can progress to respiratory failure. This is the basis of clinical presentation of acute cartap poisoning as well as the treatment with chelators namely British Anti-Lewisite (BAL). There are only a few reports of cartap poisoning in humans.[3-5] We report a case of cartap poisoning in a 50-year-old male who presented with altered sensorium.

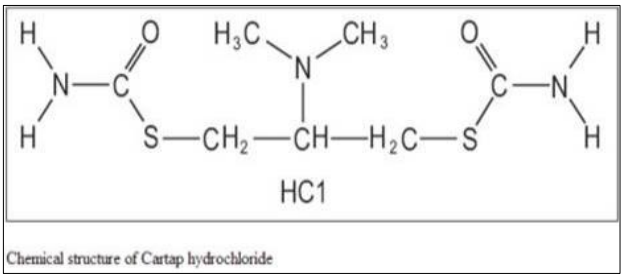

Figure 1: Chemical formula of cartap, S,S-[2-(dimethylamino)-1,3-propanediyl] dicarbamothioate.

CASE REPORT

A 50-year-old male, agricultural labourer from Punjab, India, presented with history of sudden onset altered

sensorium to emergency department. He was sprinkling pesticide at around 8 am in the morning on the day of presentation. After about 3 hours patient started experiencing giddiness and heaviness of head. He went to a local practitioner, where he was administered intravenous fluids and referred to our centre. Patient presented to our hospital after 8 hours of exposure (inhalation) of the poison. There was no history of nausea, vomiting or abdominal pain. There was no history of increased salivation, lacrimation or urinary incontinence. There was no history of seizures. Also there was no history of chest pain or palpitations.

On examination he was found to be in altered sensorium with GCS of E3V3M4. A greenish colouration (probably by chemical handling) was seen on the palms (Figure 2). The supine systolic blood pressure was 60 mm Hg and heart rate was 62 beats per minute. Respiratory rate was 28/min. Saturation by pulse oximeter was 90%. Pupils were 4.5 mm in size, equal, round, bilaterally reacting to light. There was no external evidence of trauma. On systemic examination, harsh vesicular breath sounds were heard. There was no respiratory paradox. On neurological examination, neck rigidity, Brudzinski and Kernig's signs were absent. Planters were flexor bilaterally. Examination of all other systems was normal.

Figure 2: Patient's hands stained with cartap.

Acid base gas analysis revealed partial pressure of oxygen (PaO_2) of 74.9 mmHg, oxygen saturation (SpO_2) of 91.2%, and partial pressure of carbon dioxide ($PaCO_2$) 41.4 mmHg. No academia/alkalemia were present. Chest radiograph was normal. Electrocardiogram showed normal sinus rhythm without any atrio-ventricular dissociation. Haemogram, serum electrolytes, renal and liver function tests were found to be normal. Urine output through foleys was adequate. A nasogastric tube was inserted and gastric lavage was done using normal saline. Patient was administered parenteral fluids, inj. atropine 3 mg i.v. bolus followed by infusion @1 mg/hour, inj. PAM (pralidoxime) 30 mg/kg bolus followed by infusion @8 mg/hour, considering a provisional diagnosis of organophosphate poisoning. Patient was also started on ionotropic support with dopamine infusion. Patient was monitored on cardiac monitor for any signs and symptoms of atropine toxicity and slowly tapered off the ionotropes after adequate blood pressure levels were achieved and maintained.

As the patient's condition did not seem to improve on the on-going drugs, a repeat enquiry into the cause of poisoning was made and after about 27 hours of the poisoning the patient's relatives brought the empty pack of the poison which mentioned 'cartap hydrochloride'4%w/w. Antidote (BAL 40 mg IM) was arranged and administered thereafter. Atropine and PAM infusion was stopped gradually thereafter. Within 12 hours patient's sensorium improved remarkably. Patient was kept under observation for six days and was discharged on day 7 after counselling and in stable condition.

DISCUSSION

Self-poisoning with newer agents is an emerging problem for the emergency physicians and toxicologists.[6] There is insufficient data on the clinical features, biochemical abnormalities and case fatality for these agents. Similar is the case with cartap hydrochloride poisoning. Although cartap is considered to be a low toxicity poison, severe fatalities have been reported.[7] The toxicity of cartap gets enhanced while the patients concomitantly consume foods or drugs of P450 inhibitor.[5] Further the toxicity is enhanced if the amount consumed is more than 75 mL of solution containing 50% cartap along with alcohol. The concentration of cartap in the formula is an important factor determining prognosis.[8]

Use of cartap began in Japan from where it was exported to India after a commercial agreement with Japan in 1988. Cartap comes in various brand names e.g. 'padan' in Japan where it was first used to 'chemdan', 'mantar', 'cartapvip', 'chetak', 'sudan', 'trishul' etc. Two formulations are available in India: '4% granule' and '50% water soluble powder' from the technical grade product. The 4% granule formulation is used mainly for control of paddy and sugarcane pest. The other formulation is used for control of diamond black moth on cabbage and cauliflower.[1] WHO has set the recommended 'maximum acceptable daily intake level' for CHC as 0.05mg/kg BW.[1] The WHO as a guideline has classified CHC as a moderately hazardous poison.[1] Is a an analogue of natural product 'nereistoxin' which is a potent insect neurotoxin isolated from annelid *Lumbriconereis heteropoda.*.

Cartap causes calcium dependent contracture in isolated mouse and rabbit phrenic nerve diaphragms through inhibition of the [^{3}H]-ryanodine binding to the Ca^{2+} release channel in the sarcoplasmic reticulum. This can lead to extracellular Ca^{2+} influx and induction of internal Ca^{2+} release. Cartap induced reactive oxygen species generation through a calcium dependent mechanism may play a role in contracture and myofiber injury of diaphragm ultimately leading to respiratory

failure and death in rabbits.[2] Also nereistoxin (metabolite of cartap) acts by neuromuscular blockade through inhibition of the postsynaptic nicotinic acetylcholine receptor ion channel which can lead to the convulsions, respiratory failure and the subsequent death in severe cases.[8-10]

Major cause of death is respiratory depression. Other symptoms include headache, palpitation, nausea, vomiting, flushed face, irritation or nose, throat eyes and skin, dyspnoea, mydriasis.[1,8] There are only a few reports of human cartap poisoning in the literature. However, this is probably the first case report of inhalational poisoning caused by cartap 4% concentrated form. Namera et al reported an 83-year-old woman with suicidal cartap poisoning by ingestion of cartap.[11] Gastric lavage was done after 3 hours of presentation and she recovered completely with supportive management. Kiyota et al reported a case in a woman who ingested Padan solution containing 50% cartap.[12] She presented with loss of consciousness probably after 45 minutes of ingestion. Gastric lavage was done and she recovered consciousness 8 hours after ingestion.

Cartap poisoning is likely to be misdiagnosed as organophosphate or organochlorine poisoning as it mimics many of the clinical features.[5] However; the management of these two is quite dissimilar. Cartap poisoning is managed with gastric lavage and supportive care along with antidotes in special cases. Sodium dimercaptopropane sulfonate (DMPS) and sodium dimercaptosuccinate (DMS) are effective antidotes that completely antagonize the respiratory depression caused by these compound.[1] At present the recommended antidotes for cartap poisoning are an intravenous injection of 100-200 mg of L-cysteine (L-cysteine hydrochloride injection USP, 50 mg/ml) or an intramuscular injection of 20-60 mg of BAL (Dimercaprol; 2, 3-dimercapto propanol).[1]

In this case we used 40 mg of BAL parenterally. Within 12 hours patient's sensorium improved remarkably. Patient was kept under observation for 6 days and recovered successfully without any complications. Patient was discharged on day 7 in stable condition.

Learning points

- Cartap poisoning can be misdiagnosed as organophosphate or organochlorine toxicity. Early identification of cartap poisoning is important to prevent fatality due to respiratory failure.
- The role of BAL and N-cysteine is not well established. However in case of acute cartap poisoning, after gastric lavage these antidotes can be considered with some positive evidence of beneficial effect.

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