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Cartap Hydrochloride Poisoning Causing Respiratory Failure and Seizures

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Authors' contributions

This work was carried out in collaboration between all authors. Author SRS wrote the draft of the manuscript. Author MBS managed the literature searches. Author HK designed the managed literature searches and contributed to the correction of the draft. Author MS supervised the work. All authors read and approved the final manuscript.

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Case Study

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ABSTRACT

Cartap hydrochloride is a commonly used low toxicity insecticide. It is a thiocarbamate with the chemical formula $C_7H_{16}ClN_3O_2S_2$ and a nereistoxin analogue. Major formulations available in India are cartap hydrochloride 4% GR (granules) and cartap hydrochloride 50% SP (soluble powder). We report regarding a 30 year old male patient who presented to the emergency department with alleged history of ingestion of large amount of cartap hydrochloride along with alcohol with intention of suicide. Patient developed hiccups, nausea, vomiting, dyspnea and 2 episodes of generalized tonic clonic seizures. Patient required mechanical ventilation for a period of 5 days and infusion of N-acetyl cysteine.

Toxic effect of Cartap hydrochloride is predominantly through dose-dependent inhibition of [(3)H]-

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ryanodine binding to Ca^{2+} release channel in the sarcoplasmic reticulum and promotion of Ca^{2+} influx outside the cells and induction of Ca^{2+} release inside the cells. This is the basis of clinical features of acute poisoning and treatment with British Anti Lewisite and sodium dimercaptopropane sulfonate.

Keywords: Cartap hydrochloride; nereistoxin; insecticide.

1. INTRODUCTION

Cartap is a thiocarbamate pesticide and an analogue of nereistoxin. It was first introduced in Japan (1967) and is commonly used to control chewing and sucking pests and also caterpillars [1]. Insects after administration discontinue feeding and die due to starvation. Its basic chemical structure is *S, S*-[2-(dimethylamino)-1, 3-propanediyl] dicarbamothioate and is normally used as the hydrochloride (cartap hydrochloride) [Fig. 1]. This pesticide was the first commercial insecticide derived from the structure of a natural toxin (nereistoxin), a neurotoxin isolated from the marine annelid Lumbriconeresis heteropoda [2]. It is known to be highly effective with relatively low toxicity and is a low-residue pesticide used in rice and sugarcane fields. Oral LD_{50} in the monkey **is** of 100-200 mg/kg body weight which is high compared to other pesticides [3].

The use of cartap in India started in 1988 after an agreement with which technical grade product was imported from Japan. Formulations manufactured in India are granule form (4%) and water-soluble powder (50%) form [4]. Powder form (50%) is used in cabbage and cauliflower crops for control of diamond black moth while granule form (4%) for controlling pests in paddy and sugarcane. In 1978 WHO classified cartap as moderately hazardous product [4]. We report regarding a patient who consumed around 50 grams of cartap mixed in alcohol in an attempt to commit suicide.

2. CASE REPORT

A 30 year-old man was brought to Emergency room with hiccups, 2 episodes of generalized tonic clonic seizures, severe shortness of breath and frothing from mouth with gasping for breath. As Glasgow Coma Scale (GCS) was 5/15, patient was intubated and shifted for mechanical ventilation in Intensive Care Unit. History from relatives' revealed consumption of around 100 grams of Cartap powder (50%) mixed with alcohol 2 hours ago. Past history is significant for 2 suicidal attempts by consumption of phenol and blade cutting over the wrist in the past 3 years with non-compliance for psychiatric treatment.

As the condition of the patient deteriorated in a local clinic, he was referred to our hospital. Relatives denied illegal drug use but permitted to conduct blood tests for them. His physical examination during admission was remarkable for continuous hiccups, fever (39°C), hypotension (BP: systolic 70 mm of Hg), and increased respiratory (36/min) and decreased heart (40/min) rates.

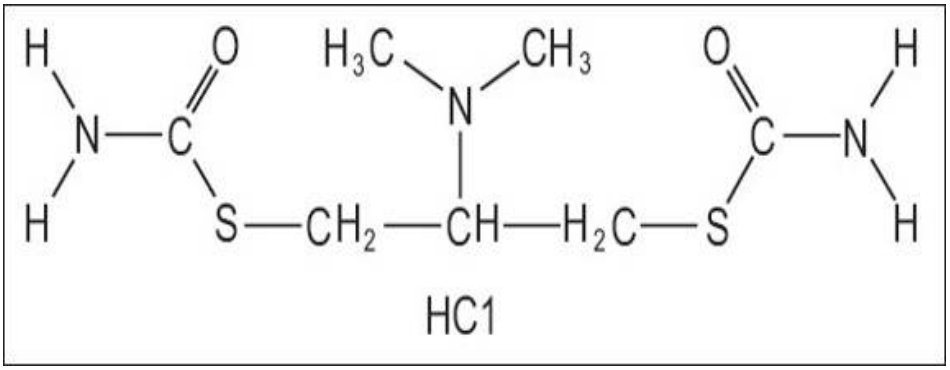

Fig. 1. Chemical structure of cartap

Systemic examination showed bilateral coarse crepitations. Gastric lavage was done and chest radiography showed alveolointerstitial infiltrates. Patient was started on prophylactic antibiotics due to fever and respiratory signs. Patient was started on atropine initially as poison consumed by patient was not available with relatives and pseudocholinesterase was extremely low (1013U/l from an external laboratory). Patient had bradycardia, excessive secretions in endotracheal tube and sweating. Atropine was stopped after 24 hours as the reports were normal and patient did not have any symptoms of cholinergic excess. Patient was given a total of 15 g of N-acetyl cysteine as treatment.

Plasma, urine, and gastric lavage samples were sent for analysis. Investigations revealed total white blood cell count of 17,100 /mm^3 (Neutrophils 50%, Lymphocytes 30%, ESR 52 mm/hr.), Hemoglobin of 15 mg/dl and platelet count was 199 × 10^3/ microliter. The arterial blood gases had pH of 7.35, a PO2 of 60 mmHg, PCO2 of 35.5 mmHg and 17.9 mmol/l of bicarbonate. Renal function test and liver function test was normal. ECG showed bradycardia and ST –T changes in leads 3 and aVF. Echocardiography was normal with ejection fraction of 60%.

Mechanical ventilation was continued with PEEP of 7 cm of H20. Condition of patient suddenly deteriorated on 2nd day with oliguria and shock. Patient required inotropic support and crystalloids. Condition of patient improved progressively and was extubated on day 4 with continuation of antibiotics for a period of 5 days. White blood cell count was 9,100 /mm^3 (Neutrophils 60%, Lymphocytes 25%, ESR 52 mm/hr.) on day 6. Patient was discharged with a follow up after 1 week.

3. DISCUSSION

The toxicity of cartap is believed to be low and fatal cases occur uncommonly. There are very few case reports describing cartap causing respiratory distress requiring mechanical ventilation and recovery after treatment. 4 case reports, including fatal cases in two reports [5,6] and 2 nonfatal cases have been published. Namera et al. [7] published regarding an 83-year-old female with suicidal ingestion of Padan (4% cartap), presenting with coma and receiving gastric lavage 3 hours after ingestion and recovered with supportive treatment. Kiyota et al. [8] reported regarding a female who took Padan (50% cartap) with loss of consciousness and recovered consciousness 8 hours after ingestion with treatment.

Kurisaki et al. [9] reported regarding a 35-year-old man who presented with 13 g of Padan (75% cartap) poisoning, hypoxemia and decreased consciousness. Patient developed multiorgan failure, DIC and expired on 5th day. Cartap exerts primary effect by increasing extracellular Ca^{2+} influx and increasing internal Ca^{2+} release [10,11]. Cartap inhibits [^{3}H]-ryanodine binding to the Ca^{2+} release channel in the sarcoplasmic reticulum in dose-dependent manner. Cartap-induced contracture to some extent is due to inhibition of Ca^{2+} pump protein in sarcoplasmic reticulum Ca^{2+} ATPase which would cause unloading of calcium from sarcoplasmic reticulum.

Liao et al. [3] concluded in their study that the effect of cartap was due to persistent diaphragmatic contraction and was not due to neuromuscular paralysis resulting in respiratory failure. Our patient presented with persistent hiccups initially which may be due to diaphragmatic contractions. It is believed that Cartap is of a lower potency to nereistoxin. Bensultap, thiocyclam, and thiosultap are other nereistoxin analogues available. Mechanism of action described by Gyori et al. [12] in Toxicology *in vitro* showed postsynaptic nicotinic acetylcholine receptor (AChR) inhibition of ion channels. Several sulfhydryl-containing compounds (L-cysteine, D -penicillamine) in experimental animals have shown to delay the onset of symptoms from cartap hydrochloride poisoning [1,13,14].

Oximes are nucleophilic agents that reactivate the phosphorylated acetylcholinesterase by binding to the organophosphorus molecule [15]. Use of oximes in organophosphorus poisoning is conflicting and controversial. Lifshitz et al. [16] described 26 children aged 1–8 years with severe Carbamate poisoning. On treatment with atropine and oximes, all children recovered within 24 hours, and it was concluded that there is no danger of clinical deterioration when victims of Carbamate poisoning are treated with oximes.

4. CONCLUSION

Cartap poisoning is very rare and cases with fatal toxicity occur very rarely. Our case report establishes the following. 1) Patient presenting with hiccups may be due to diaphragmatic contraction and later causing respiratory failure.

2) N-acetyl cysteine usage improving the condition of patient.

CONSENT

All authors declare that 'written informed consent was obtained from the patient (or other approved parties) for publication of this case report.

ETHICAL APPROVAL

All authors hereby declare that this case report was approved by the appropriate ethics committee and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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