Rhabdomyolysis and acute kidney injury associated with thiocyclam hydrogen oxalate (Evisect) poisoning

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Abstract
Thiocyclam hydrogen oxalate (Brand name: Evisect) is an insecticide with anti-cholinergic and cholinergic properties. Although there are few case reports and a case series of human toxicity of nereistoxin analogue insecticide such as cartap hydrochloride poisoning published in the literature, poisoning with thiocyclam hydrogen oxalate (Evisect), an another analogue of nereistoxin with its own molecular formula is only heard in animals, such as Nubian goats. Herein, we report a patient presented with rhabdomyolysis and acute kidney injury without significant symptoms of acute cholinergic syndrome following self-ingestion of thiocyclam hydrogen oxalate (Evisect) and he made an uneventful recovery with prompt supportive care.

Keywords
Evisect, rhabdomyolysis, thiocyclam hydrogen oxalate, poisoning, acute kidney injury

Date received: 3 March 2020; accepted: 10 August 2020

Introduction
Thiocyclam hydrogen oxalate (Evisect) is a broad-spectrum synthetic insecticide used to control the sucking and chewing pets on a variety of crops. It contains thiocyclam hydrogen oxalate, and its chemical name is N,N-dimethyl-1,2,3-trithian-5-amine hydrogen oxalate. It was initially prepared by Sandoz Laboratories, Basle, Switzerland. It has been usually supplied as a soluble powder or as granules. As it is degraded rapidly, residues do not persist in the environment.1

Thiocyclam hydrogen oxalate acts as acetylcholine receptor agonist at low concentrations and antagonist at high concentrations without affecting the cholinesterase activity. Even though it was well demonstrated in the animal model that it is known to cause hepatic, renal, cardiac and lung injury following an ingestion,2 a little is known about features of systemic toxicity of thiocyclam hydrogen oxalate (Evisect) poisoning in humans following an oral ingestion as the literature related to toxicity caused by Evisect insecticide in human is sparse. Herein, we report on a patient with deliberated self-ingestion of thiocyclam hydrogen oxalate (Evisect) associated with rhabdomyolysis and acute kidney injury (AKI).

Case presentation
A 38-year-old Sri Lankan male presented to the Jaffna Teaching Hospital, following an ingestion of one packet (50% w/w, 100 g) of thiocyclam hydrogen oxalate (Evisect) dissolved in water, taken 15 h prior to arrival. He strongly denied co-ingestion of any other substances including organophosphate, illicit drugs, liquor or pharmaceuticals. He experienced abdominal discomfort and nausea for a short period immediately following ingestion and then he had been asymptomatic for about next 12 h. There after he started to develop nausea, vomiting and severe myalgia associated with diffuse abdnominal pain. At the same time, he also noticed that the amount of urine voiding had been declining progressively and dark in colour. He had no characteristic symptoms suggestive of anti-cholinergic or cholinergic toxidrome. His past medical history was unremarkable, and he

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Eosinophils (×10⁹/L) 0.02–0.5 0.16 0.18 0.10 0.71 0.46 0.52 0.22
Lymphocytes (×10⁹/L) 1.0–3.0 1.99 1.02 1.04 1.19 1.77 1.20 1.44
Basophils (×10⁹/L) 0.02–0.1 0.06 0.02 0.03 0.05 0.04 0.06 0.04
Monocytes (×10⁹/L) 0.2–1.0 1.16 1.11 1.35 1.54 1.02 0.69 0.29
Neutrophils (×10⁹/L) 2.0–7.0 13.28 6.86 7.80 8.45 6.05 5.85 5.18

Table 1. Serial full blood counts with differentials.

| WBC (×10⁹/L) | Reference range | Day 0 | Day 1 | Day 2 | Day 4 | Day 8 | Day 11 | Review at 2 weeks |
|--------------|----------------|-------|-------|-------|-------|-------|-------|------------------|
| 16.6         | 4.0–11.0       |       |       |       |       |       |       |                  |
| 9.28         | 2.0–7.0        |       |       |       |       |       |       |                  |
| 10.4         | 1.0–3.0        |       |       |       |       |       |       |                  |
| 11.9         | 0.2–1.0        |       |       |       |       |       |       |                  |
| 9.3          | 0.02–0.5       |       |       |       |       |       |       |                  |
| 8.6          | 0.02–0.1       |       |       |       |       |       |       |                  |
| 7.2          | 11.8–14.8      |       |       |       |       |       |       |                  |
| 12.5         | 36–44          |       |       |       |       |       |       |                  |
| 12.8         | 76–96          |       |       |       |       |       |       |                  |
| 12.4         | 150–400        |       |       |       |       |       |       |                  |

WBC: white blood cell; Hb: haemoglobin; HCT: haematocrit; MCV: mean corpuscular volume.

Discussion

Nereistoxin is a natural substance which was initially isolated from the marine *Lumbriconereis heteropoda*, and its primary action is inhibition of postsynaptic nicotine acetylcholine ion channels. The nereistoxin analogues currently in use include cartap (thiocarbamate), bensultap, thioyclam and thioulant.

Thiocyclam hydrogen oxalate (Evisect) is a broad-spectrum nereistoxin analogue insecticide used widely for agricultural applications. This is a biological contact insecticide developed in Switzerland in the late 1960s. Evisect is available as a soluble powder and granules. This compound is not known to be injurious to plants with the exception of certain varieties of apple.

Thiocyclam hydrogen oxalate shows cholinergic effects at low concentrations and anti-cholinergic effects at high concentrations without affecting the cholinesterase activity. This insecticide is an antagonist at high concentration, blocking cholinergic transmission resulting in paralysis and insect death. This insecticide is metabolically converted to nereistoxin in the insect and interacts with nicotine acetylcholine receptors.

There are few case reports and a case series of human toxicity of cartap hydrochloride poisoning published in the literature mostly from Japan and India. Reported symptoms of cartap poisoning include acute cholinergic syndrome (such as vomiting, salivation and nausea) with respiratory failure resembling organophosphate poisoning.

Toxicity of thiocyclam hydrogen oxalate (Evisect) on humans has not been reported up to date. This is the first case report of Evisect toxicity on humans, and it was associated with severe rhabdomyolysis and AKI. His initial biochemical profile showed disproportionately very high serum creatinine compared to blood urea along with elevated CPK suggestive of kidney injury probably due to rhabdomyolysis. In addition, it was also further supported by raised lactate dehydrogenase (LDH) and high transaminases with aspartate transaminase (AST) > alanine transaminase (ALT) indicating muscle origin. Changing pattern of activity.
AST and ALT (ALT > AST) observed after the sixth day of illness was indicating that progress of rhabdomyolysis had been ceased or significantly reduced and half-life of AST is shorter than ALT. Although it was well documented that car tap poisoning is known to cause cholinergic syndrome, our patient with thiocyclam hydrogen oxalate poisoning did not show typical features of cholinergic syndrome or features of respiratory failure during the course of illness.

The toxicity of Evisect was studied in Nubian goats with the deferent levels of exposure. In this study, the renal biopsy showed glomeruli were shrunken demonstrating widening of Bowman’s space where the tuft lobulated, disappeared or infiltrated with lymphocytes. There were slight renal tubular dilatation and necrosis also noted particularly in medulla.\(^2\) Even though such findings could not be extrapolated to human beings, study on this animal model failed to show any evidence of rhabdomyolysis which was the major concern in our case. As renal biopsy has not been performed in this case, direct toxicity of renal tissues by Evisect in human is still obscure.

In an ideal setting, analytical confirmation of exposure to thiocyclam hydrogen oxalate is carried out by liquid chromatography or mass spectrometry. However, the lack of feasibility of these sophisticated investigations is a major limitation of this case report. An intravenous l-cysteine or an intramuscular injection of British anti-Lewisite is used as an antidote for cartap poisoning,\(^4\) but their role in thiocyclam hydrogen oxalate poisoning is not known.

### Conclusion

The literature related to toxicity caused by thiocyclam hydrogen oxalate (Evisect) insecticide in human is sparse. This case demonstrates that thiocyclam hydrogen oxalate toxicity is associated with rhabdomyolysis and AKI in humans.

### Acknowledgements

The authors acknowledge the patient who agreed for the publication of his case.

### Author contributions

N.S. and R.M. collected all data from regional hospital and initiated to write this case report. T.K. contributed revision of the manuscript and references. All authors read and approved the final manuscript.

### Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship and/or publication of this article.

### Ethics approval and consent to participate

The institution does not require ethical approval to publish individual case report.

### Funding

The author(s) received no financial support for the research, authorship and/or publication of this article.

### Informed consent

Informed written consent for the publication was obtained from the patient. The patient has given written informed consent for the publication of his case report.

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