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## INTRODUCTION

Closantel is a broad-spectrum antiparasitic agent used against several species and developmental stages of trematodes, nematodes and arthropods. The classical signs of closantel toxicity in animals include blindness, paresis and ultimately death (1). In humans, except for eleven cases of women in Lithuania who temporarily lost their eyesight after using closantel (the drug was mistakenly given to treat endometritis) (2); no cases of blindness with closantel have been reported subsequently. We report three cases of accidental ingestion of this veterinary product leading to blindness.

## CASES SERIES

### Case 1

A 3-year-old girl presented with sudden onset of blindness, 24 hours after accidental ingestion of an unknown amount of closantel. His father, who uses the product at his farm, forgot the open bottle on the table. She had bilateral mydriasis with abolition of pupillary reflex. The fundal photograph showed severe papilloedema. The Magnetic Resonance Imaging of the brain and the orbit was normal. The diagnosis of toxic optic neuropathy was established because of normal radiological investigations and biological exams. The Poison Control Centre of Morocco advised the administration of oral vitamins B1, B6 and B12; with a gradual improvement of blindness two months later.

### Case 2

A 40-year-old female presented with progressive blindness one week after accidental ingestion of closantel (by decanting the drug in a solution kept in a bottle of mineral water). The fundal photograph was normal. The visual field showed scotoma with deterioration of cones and rods in the retina. Laboratory tests were normal. Another cause of blindness could not be eliminated in the absence of radiological investigations. The outcome of the patient was unknown.

### Case 3

A 44 year-old male ingested one dose of closantel, in order to treat intestinal parasitosis. He developed nausea and weakness and he stopped the medication. The patient became blind, one week after the initial ingestion of the product. The patient has not had an eye examination because of the absence of adequate hospital facilities in the area where he lives and was referred to an ophthalmologist but he was lost to follow up.

## CONCLUSIONS

- There are many research questions that need to be answered about the unusual toxic cause of optic neuropathy after ingestion of closantel
  - Range of toxicity of closantel in the human ?
  - Toxicokinetic of closantel?
  - Pathogenesis of blindness after closantel poisoning ?
  - Place of vitaminotherapy in the treatment of closantel poisoning?
- It should be the goal to prevent such accidents, based on a broad public education on the use of veterinary products.

## DISCUSSION

The halogenated salicylanilides are a large group of compounds developed mainly for their antiparasitic activity in animals. Several halogenated salicylanilides with potent antiparasitic activity have been synthesised of which only closantel, niclosamide, oxyclozanide, rafoxanide and resorantel are commercially available (1).

In Morocco, closantel is available in an injectable form (Caliersantel) and in an oral form (Flukiver) (3).

In studies in rats and sheep, closantel was shown to be strongly bound to the plasma proteins. The compound was poorly metabolized, mainly to 3- and 5- monoiodoclosantel. About 90% of the administered dose was excreted in the faeces, and about 90% was unchanged (4,5).

Clinical signs of closantel toxicity include inappetence, ataxia, paresis, recumbency, and blindness. The first ophthalmological signs are absence of pupillary light reflexes and papilloedema. Loss of light reflexes indicates optic nerve or retinal damage, or both (6)

One study on sheep showed that pathological changes in the optic nerves nature and progression of the lesions showed initial myelin vacuolation leading to Wallerian degeneration and eventual irreversible fibrosis and contraction of the nerve. A common pathogenesis for the optic neuropathy, namely initial myelin oedema followed by swelling and compression of the nerve within the bony canal, has been proposed. It would seem that closantel has a direct retinotoxic effect in small stock (6).

Histologically, widespread spongy changes (status spongiosus) in the central nervous system, optic neuropathy and retinal degeneration have been described (6)

The anthelmintic spectrum of closantel has been linked to the compound's ability to uncouple oxidative phosphorylation, but it is not known whether this mechanism could account for the toxic effects in sheep and goats (1)

The toxicity of closantel in human was poorly assessed. Limited clinical reports were available from 33 patients who were treated with a single oral or parenteral dose of closantel at 2.5 to 10 mg per kg of body weight. In all treatment groups, side effects such as diarrhoea, drowsiness and blurred vision were observed [7,8]. In 1993, 11 women in Lithuania were temporarily blinded after using an anthelmintic drug that should only be used in veterinary medicine but was given for a gynaecological complaint (2)

The diagnosis of toxic optic neuropathy was established in the case 1 because of the notion of closantel accidental ingestion, data of ophthalmological examination, normal radiological investigations and biological exams. In the other cases, because of lack of investigations, this diagnosis still the most probably diagnosis of blindness.

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