BLINDNESS CAUSED BY SELF-TREATMENT WITH VETERINARY DRUG CLOSANTEL

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Objective

Flukiver Combi® (closantel 50 mg/mL and mebendazole 75 mg/mL) is a veterinary drug used as anthelmintic for cattle, sheep and goats. The recommended treatment is a single dose of 1 mL/5 kg (closantel 10 mg/kg and mebendazole 15 mg/kg). Mebendazole is used in human medicine too, but the salicylanilide-derived component closantel is only used in veterinary medicine (1).

Case Report

Patient: **59-year-old man**

Route of exposure and dose:

The patient ingested 4 mL Fluciver Combi® three times daily for 3 days on purpose to cure himself.
Total dose of 36 mL results in closantel 30 mg/kg and mebendazole 45 mg/kg.

Time of admission:

approximately 4 days after last dose

Clinical features:

➢ **Initial symptoms**:

scotomata not otherwise specified

➢ **Eye examination at time of admission**:

Visual acuity 0,3 (right)
0,4 (left)

Ocular tension 19 mmHg (right)
18 mmHg (left)
(normal 10 - 21 mmHg)

Front section and fundus inconspicuous on both sides

Static perimetry:

- Scotomata in the total 30° visual field
- Mean visual field defect: 8,8 dB (right)
  11,0 dB (left)

Visually evoked cortical potentials:

- VEP could not be recorded reproducibly

Other laboratory findings were inconspicuous.

Treatment and course:

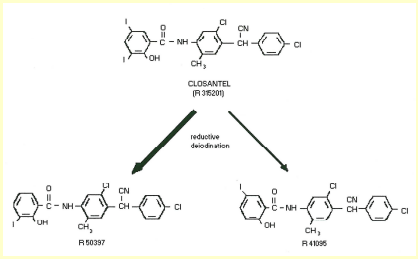
- Glucocorticoids inefficient;
- Total blindness 10 days after last dose;
- Plasmapheresis;
  analysis of plasma samples is in process;
- Recovery of visual acuity to 0,6 was reported six weeks after last dose.

Mechanism of action

➔ Membrane damage due to closantel acting as a hydrogen ionophore resulting in the uncoupling of electron transport-associated phosphorylation

Damage of the optic nerve

➔ Development of oedema and vacuolisation of the myelin sheaths followed by compression of the nerve within the osseous part of the nerve canal resulting in Wallerian degeneration, fibrosis, and atrophy



Metabolic pathways of closantel in sheep
(Ref. WHO Food Additives Series 27)

Animal Pharmacokinetic Data of Closantel

Absorption

- Oral bioavailability in sheep and cattle 50 % (1)
- Maximum plasma levels 24 to 48 hours after p.o. or i.m. application (1)

Distribution

- Plasma protein binding 99 % (1)

Metabolism

- Biotransformation to 3- and 5-monoiodoclosantel isomers (only 2 % of the dose) (1)

Elimination

- Biliary excretion mainly unchanged (80 % of the dose) (1)
- Half-life in sheep and cattle 16 to 23 days (1)

Animal Toxicity of Closantel

Therapeutic Range

- Four- to sixfold therapeutic doses were tolerated without symptoms in sheep and cattle, respectively (1)

Toxic Effects

- Anorexia, movement disorders, general asthenia, impaired vision or blindness (1)

Toxic Dose

- LDLo Goat, Sheep p.o. 70 mg/kg (RTECS)
- LDLo Cattle p.o. 82,5 mg/kg (1)
- LD50 Rat p.o. 262 mg/kg (RTECS)

Conclusions

➢ This case confirms the report of ‘t Hoen and Hodgkin (2) that closantel causes reversible blindness in humans. Obviously, humans are more sensitive to this toxic effect than animals.

➢ The long-lasting effect correlates with the slow elimination of the unchanged drug.

➢ Furthermore, the case indicates the remarkable risk of self-treatment with drugs unapproved for human use.

Literature

(1) Homepage CliniPharm/CliniTox - Institute of Pharmacology and Toxicology, University of Zurich http://www.vetpharm.uzh.ch/wir/00005780/8658__F.htm; (2) ‘t Hoen E, Hodgkin C. Harmful human use of donated veterinary drug. Lancet 1993; 342(8866):308-9.