

# Reversible blindness after erroneous prescription of closantel: A case report

Hamed Cheraghmakani<sup>1</sup>, Reza Jafari<sup>1</sup>, Elahe Karimpour-razkenari <sup>2</sup>, and monireh Ghazaeian<sup>2</sup>

<sup>1</sup>Mazandaran University of Medical Sciences Faculty of Medicine

<sup>2</sup>Mazandaran University of Medical Sciences Faculty of Pharmacy

September 25, 2021

## Abstract

A 20-year-old girl referred with vision loss upon closantel use. Plasma exchange and high-dose corticosteroid pulse therapy were administered. A 2.5-year follow-up showed improved vision and increased layer thickness of the peripheral nerve fiber. Early treatment with plasma exchange and high-dose corticosteroid therapy can be beneficial to reverse closantel toxicity.

## Reversible blindness after erroneous prescription of closantel: A case report

Hamed Cheraghmakani<sup>1</sup>, Elahe Karimpour-razkenari <sup>2</sup>, Reza Jafari<sup>3</sup>, Monireh Ghazaeian <sup>\*4</sup>.

<sup>1</sup> Department of Neurology, Faculty of Medicine, Mazandaran University of Medical Sciences, Sari, Iran.

<sup>2</sup>Department of Clinical Pharmacy, Faculty of pharmacy, Mazandaran University of Medical Sciences, Sari, Iran.

<sup>3</sup> Department of Ophthalmology, Faculty of Medicine, Mazandaran University of Medical Sciences, Sari, Iran.

<sup>4</sup> Pharmaceutical Sciences Research Center, Department of Clinical Pharmacy, Faculty of Pharmacy, Mazandaran University of Medical Sciences, Sari, Iran.

**\*Corresponding author:** Monireh Ghazaeian

**E-mail:**ghazaeianm@gmail.com

## Reversible blindness after erroneous prescription of closantel: A case report

### Key clinical message:

Wrong prescriptions of closantel can cause toxic effects on central visual acuity and optic nerve. Early initiation of plasma exchange and corticosteroid pulse therapy can reverse the destructive effects of closantel on retina ganglion cells over time.

## Abstract

A 20-year-old girl referred with vision loss upon closantel use. Plasma exchange and high-dose corticosteroid pulse therapy were administered. A 2.5-year follow-up showed improved vision and increased layer thickness of the peripheral nerve fiber. Early treatment with plasma exchange and high-dose corticosteroid therapy can be beneficial to reverse closantel toxicity.

**Keywords :** Closantel, Blindness, Toxicity.

## Introduction

Halogenated salicylanilides are well-known for their anti-parasitic effects. The most famous medicine in this category is closantel, which is used worldwide against *Haemon chus* spp. and *Fasciolasp.* infestations in sheep and cattle (1, 2).

Animal studies indicate that the oral bioavailability of closantel in sheep and cattle is about 50% and that the maximum plasma concentrations (C<sub>max</sub>) are reached 24–48 h after administration with extensive binding to plasma albumin (> 97%). Moreover, the elimination half-life is from 7 days to 3 weeks depending on the animal (3,4). Animals' ocular studies after closantel intoxication have shown edema in the intracanalicular portion of the optic nerve, causing demyelinated axons, fibrosis of the optic nerve, and retinal degeneration resulting in mydriasis, loss of pupillary reflexes, and bilateral blindness (5,6). Besides, retina injury leads to the thinning of photoreceptive cells (7).

This study reports a rare case of blindness after wrong administration of closantel to treat *Fasciola hepatica* infection in a young girl, who successfully managed with drug discontinuation, plasmapheresis, and corticosteroids.

## Case presentation

A 20-year-old girl with the primary complaints of bilateral blurred vision and decreased color vision, progressing from 3 days earlier, was admitted to the emergency department on Aug 16, 2018. She had a history of *Fasciola hepatica* from 20 days earlier. Although her specialist had prescribed triclabendazole, she was given closantel as an alternative by mistake. She took 500 mg of closantel twice daily for three days. On the second day of administration, she was unable to see fine details and lost vision sharpness bilaterally. On the third day, her problem progressed to blurred vision followed by color blindness.

There was no systemic illness and her physical examination was normal, including central nervous system and abdominal examination. On primary eye examination, the intraocular pressure of both eyes appeared normal without any refractive error. Fundus examination showed a normal macula appearance. She had the bilateral pale disc and optic atrophy with sluggish papillary reaction to light, and negative RAPD (relative afferent pupillary defect) was detected.

In the Humphrey visual field test, she showed a complete visual field defect in the central 24-degree vision. Optical coherence tomography (OCT) and retinal nerve fiber layer (RNFL) thickness in the Temporal-Superior-Nasal-Inferior-Temporal (TSNIT) map revealed a thinning neural area of both eyes and a temporal fiber thinning in the right eye (Fig. 1). Inferonasal and superonasal fiber had a good condition in both eyes. However, the superotemporal and inferotemporal peri-papillary fiber of the right eye had prominent thinning. Together, RNFL thinning was dominant in the right eye. Inferior to superior hemispheric asymmetry in the RNFL thickness and ganglion cell layer thickness were not significant. Fundus autofluorescence was normal. Fluorescein angiography of both eyes had no defects in the vascular filling.

Plasmapheresis was performed immediately in an emergency department, and the course of treatment consisted of five sessions of apheresis. She also underwent corticosteroid pulse therapy with methylprednisolone (1000 mg/day) for three consecutive days. At discharge, after 14 days of treatment, she could see the shape of people or objects, and notice their movement. In the course of the five-month follow-up, her visual field was gradually improved with the defect being confined to central 10 degrees. The vision enhanced from counting fingers one meter to counting fingers 6 meters. After an 18-month follow-up, her vision improved to counting fingers 8 meters. Furthermore, after a 2.5-year follow-up, the peripheral nerve fiber layer showed the highest improvement in superior and inferior arcuate fibers in the thickness analysis of the peri-papillary nerve fiber layer, a finding that was compatible with the subjective data of visual field improvement (Fig. 1, 2).

## Discussion

Closantel poisoning is usually accompanied by neurotoxicity, ophthalmic toxicity, and hepatotoxicity in

animals. There is no specific antidote for poisoning, and information is scarce for humans (7). Recent findings of closantel toxicity have shown that the toxic effects on retinal ganglion cells may harm the central visual acuity and optic nerve (8). According to our findings from RNFL and macula analysis (Fig 3), it seems that the process of repairing damages to peripheral layers occurs faster than that of damages to the central layers, which may explain the reduction of the central visual field (Fig. 2).

Wrong prescriptions of closantel for 11 Lithuanian women was the first human-documented closantel exposure, with temporarily visual acuity loss after closantel exposure (9). After 22 years, the vision loss of five of them was partially reversed without significant recovery over time (10). According to our information, the use of plasmapheresis in one case and systemic corticosteroid in another one showed significant recovery of the vision (7,11). However, the literature also reports complete vision loss because of closantel poisoning (12).

Systemic corticosteroids were used in two case reports of closantel poisoning, with different results (7,12). It seems that the time of treatment onset has a key role. Moreover, a recent case report of reversible blindness upon accidental use of closantel highlighted that immediate management with corticosteroids can have beneficial effects on visual function (13).

Corticosteroid and vitamin B12 have been routinely prescribed for some poisoning cases (7,12,14). Furthermore, plasmapheresis was used for two cases, given the pharmacokinetic property and the high protein binding of closantel (11,15).

In our case, the pre-treatment OCT scan of the macula showed a generalized and uniform reduction in neural thickness of both eyes. Her blindness was fairly treated with plasmapheresis and corticosteroid pulse, and her vision improved significantly after an 18-month follow-up. Vision improvement of both eyes may suggest that early initiation of plasma exchange and corticosteroid pulse therapy can reverse the destructive effects of closantel on retinal ganglion cells over time. Moreover, regarding pharmacokinetic characteristics (low volume distribution and high protein binding), plasma exchange can be a rational way to remove closantel.

## Conclusion

This is a case report of successful treatment of closantel-induced blindness. Early treatment with plasmapheresis and systemic corticosteroid can be considered an effective intervention to reverse the toxic effects of closantel. Besides, it seems reasonable to provide education on the use of veterinary products and to relabel this drug as forbidden for humans, given the lack of a definite antidote for it and the possibility of irreversible blindness.

## Acknowledgment:

We would like to thank Tabarestan ophthalmology clinic staffs to support our patient follow-up.

## Conflicts of interest:

The authors declare that they have no competing interests.

## Funding:

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors

## Authorship:

HCH, RJ, MGH carried out diagnostic management. EK and MGH contributed in writing of manuscript and organizing patient's files. MGH revised the manuscript. All authors read and approved the final manuscript.

## Ethics approval and consent to participate

Written informed consent for publication of their clinical details and/or clinical images was obtained from the patient/parent/guardian/ relative of the patient. A copy of the consent form is available for review by

the Editor of this journal.

## Data availability statement

The data of the study are available from the corresponding author upon rational request.

## References:

1. Swan GE. The pharmacology of halogenated salicylanilides and their anthelmintic use in animals. *J S Afr Vet Assoc* 1999;70:61-70.
2. Sargison ND. Pharmaceutical control of endoparasitic helminth infections in sheep. *Vet Clin Food Anim* 2011;27:139-56.
- 3) Lanusse CE, Virkel GL, Alvarez LI. Anticestodal and Antitrematodal Drugs. In: Riviere JE, Papich MG, editors. *Veterinary Pharmacology and Therapeutics*. John Wiley & Sons; 2018 Feb 28. P: 1081-1102
- 4) Rassouli A, Arab H, Ghezelloo Y, Shams GR. A bioequivalence study on two closantel oral suspensions in sheep: an Iranian product (fascinil®) versus flukiver® as a reference product. *Iran J Vet Med* 2013;7:263-9.
- 5) Van der Lugta JJ, Venter I. Myelin vacuolation, optic neuropathy and retinal degeneration after closantel overdosage in sheep and in a goat. *J Comp Pathol*. 2007;136:87–95. <https://doi.org/10.1016/j.jcpa.2006.11.007>.
- 6) Ecco R, Barros CS, Graça DL, Gava A. Closantel toxicosis in kid goats. *Vet Rec* 2006;159:564-6.
- 7) Kumar K, Mishra C, Anjanamurthy R, Kannan NB, Ramasamy K. Reversible blindness in a patient with closantel toxicity. *Indian journal of ophthalmology*. 2019 Oct;67(10):1768.
- 8) Kurakina ES, Ioyleva EE, Saif MA, Gavrilova NA. The damage of the optic nerve as the outcome of unintentional poisoning by closantel. *Malang Neurology Journal*. 2020 Dec 15;7(1):70-3.
- 9) Hoen ET, Hodgkin C, Milkevicius D. Harmful human use of donated veterinary drug. *The Lancet*. 1993 Jul 31;342(8866):308-9.
- 10)Asoklis R, Cimbaldas A, Augyte A, Jasinskiene E, Strupaite R. Late ocular changes after closantel poisoning in five women. *Eye*. 2018 Aug 3:1.
- 11) Koziolk MJ, Patschan D, Desel H, Wallbach M, Callizo J. Closantel Poisoning Treated with Plasma Exchange. *JAMA ophthalmology*. 2015 Jun 1;133(6):718-20.
- 12) Tabatabaei SA, Soleimani M, Mansouri MR, Mirshahi A, Inanlou B, Abrishami M, Pakrah AR, Masarat H. Closantel; a veterinary drug with potential severe morbidity in humans. *BMC ophthalmology*. 2016 Dec;16(1):207.
- 13) Khalili MR, Zareei A. Case report: restored vision after ocular Closantel intoxication and blindness. *BMC ophthalmology*. 2021 Dec;21(1):1-7.
- 14) Essabar L, Meskini T, Ettair S, Erreimi N, Mouane N. Harmful Use of Veterinary Drugs: Blindness Following Closantel Poisoning in a 5-Year-Old Girl. *Asia Pacific Journal of Medical Toxicology*. 2014 Dec 1;3(4):173-5.
- 15) Bergmann I, Frimlova G, Just S, Schaper A, Stuerzebecher A, Radamm C, Hentschel H. Blindness caused by self-treatment with the veterinary drug closantel. InXXXIII International Congress of the European Association of Poisons Centres and Clinical Toxicologists (EAPCCT) 2013 May 1 (pp. 28-31).

Fig 1. OCT findings: A; showing the thinning of external and internal layers of retinae at baseline. B: improvement in superior and inferior arcuate fibers in the thickness analysis of the peri-papillary nerve fiber layer after a 2.5-year follow-up.

A

### Hosted file

image1.emf available at <https://authorea.com/users/437414/articles/539062-reversible-blindness-after-erroneous-prescription-of-closantel-a-case-report>

B

### Hosted file

image2.emf available at <https://authorea.com/users/437414/articles/539062-reversible-blindness-after-erroneous-prescription-of-closantel-a-case-report>

Fig 2. Improvement on visual field apparent in the visual field test (right eye).

### Hosted file

image3.emf available at <https://authorea.com/users/437414/articles/539062-reversible-blindness-after-erroneous-prescription-of-closantel-a-case-report>

### Hosted file

image4.emf available at <https://authorea.com/users/437414/articles/539062-reversible-blindness-after-erroneous-prescription-of-closantel-a-case-report>

Fig 3. Macula OCT at baseline (A) and after a 2.5-year follow-up (B): Macular area was more involved in objective data in macular OCT in early and long-term follow-ups. Intra-retinal cystic changes due to outer retinal layer atrophy were noticed.

A B

### Hosted file

image5.emf available at <https://authorea.com/users/437414/articles/539062-reversible-blindness-after-erroneous-prescription-of-closantel-a-case-report>

### Hosted file

image6.emf available at <https://authorea.com/users/437414/articles/539062-reversible-blindness-after-erroneous-prescription-of-closantel-a-case-report>