Case Report

High-Dose Steroids and Pentoxifylline in Methanol-Induced Optic Neuropathy: A Case Report and Review of the Literature

Keean Nanji[a*] MD, Alex Pozdnyakov[b] MD, Teresa Semalulu[b] MD, Ameen Patel[b] MB, FRCP(C), FACP

a. McMaster University, Department of Surgery, Division of Ophthalmology, 2757King St E., Hamilton, Ontario, Canada, L8G 5E4.
b. McMaster University, Department of Internal Medicine, Hamilton Health Sciences,1200 Main St W, L8N 3Z5

Abstract

Acute methanol poisoning is known to cause significant neurological and ophthalmological sequelae. There are case series and case reports documenting the improvement of visual impairment with high-dose intravenous steroids, pentoxifylline and supportive therapy; however, there currently lacks high-quality evidence for the treatment of methanol-induced visual impairment. This article summarizes a case of methanol poisoning, the attempt to salvage vision, and summarizes the available literature regarding the management of methanol optic neuropathy.

Keywords: Methanol toxicity, Optic neuropathy, Pentoxifylline, Visual impairment

Corresponding author: keean.nanji@medportal.ca

Introduction

Acute methanol poisoning treatment algorithms provide strategies to clear toxic levels ofmethanol metabolites and manage high anion gap metabolic acidosis to prevent neurological andophthalmological sequelae. However, there are no evidence-based interventions aimed at restoring methanol-related impairment of visual function. Methanol toxicity is primarily attributed to the effects of its metabolite, formic acid. The accumulation of formic acid interferes with mitochondrial cytochrome oxidase and causes hypoxia, resulting in retinal and optic nerve toxicity.(1). Case series and reports suggest potential benefits from the use of intravenous steroids and pentoxifylline for methanol-induced optic neuropathy (2-4). This case report describes a patient with methanol-related vision loss who was treated with high-dose intravenous steroids, pentoxifylline, and supportive therapy to salvage his vision.

Case Presentation

A 70-year-old male presented to his local hospital with a decreased level of consciousness and new-onset decreased visual acuity. Prior to his visit, he engaged in four days of binge drinking, during which he ingested approximately 150 mL of methanol. He started consuming methanol 72 hours prior to presentation and stopped 24 hours prior to arrival at his local Emergency Department (ED). The onset of visual changes occurred approximately 36 hours after he started to consume methanol.

On presentation to his local hospital, he was afebrile, tachycardic and hypertensive. Hewas given 100 mEq of bicarbonate, 1 L of normal saline, 0.5 mg of midazolam and was transferred to our tertiary care center. His lab values on presentation to his local hospital and toour center can be found in Table 1. A CT head showed no evidence of acute intracranial abnormalities. An ECG demonstrated a prolonged QTc of 467 ms. The patient was givenfomepizole, leucovorin, thiamine and started on hemodialysis.

Table 1. Lab values of our patient on initial presentation and on presentation to our care center.

	On presentation to his local ED	On presentation to our ED
Sodium (mmol/L)	136	134
Chloride (mmol/L)	100	104
Bicarbonate (mmol/L)	5	5
Anion Gap (mmol/L)	31	25
Lactate (mmol/L)	11.6	2.5
pH	6.89	7.17
Osmolar Gap (mOsm/L)	Not obtained	41.7

The patient's initial bilateral best-corrected visual acuity (BCVA) was to hand motion bilaterally. Intraocular pressures were 26 and 19 mmHg in the right and left eyes respectively. Pupils were fixed and not reactive to light. Anterior segment examination revealed bilateral 2+ nuclear sclerotic cataracts. Posterior segment examination revealed a bilateral cup to disc ratio of 0.5. On day 1, his BCVA decreased to light perception bilaterally.

By hospital day 5 he was systemically well but had experienced no improvement in visual acuity. After multiple discussions with the patient and his wife, and based on our literature review of reported benefits (2, 3), he was treated with IV methylprednisolone 1g daily for 3 days followed by 40mg of oral prednisone as well as a 6-week course of 400 mg of pentoxifylline, 1000 mg of vitamin B12, 2000 U of Vitamin D and 1250 mg of calcium carbonate.

By hospital day 11, six days post initiation of steroids, his BCVA remained to light perception bilaterally, his pupils remained unreactive to light. and posterior segment examination revealed a bilateral cup-to-disc ratio of 0.1 with no pallor. Optical coherence tomography (OCT) through the retinal nerve fiber layer (RNFL) showed an average thickness of 129 microns in the right and 140 microns in the left.

There was no improvement in visual acuity 37 days following hospital admission and 32 days after starting the steroids. His pupils were persistently nonreactive to light and examination revealed bilateral cup-to-disc ratios of 0.5 without nerve pallor. OCT through the RNFL revealed a thickness of 89 and 100 microns in the right and left eyes respectively. The initial thickening of the RNFL followed by subsequent thinning is characteristic of acute swelling followed by progressive atrophy seen in methanol optic neuropathy.(5).

Discussion

We describe a case of methanol toxicity with severe visual impairment that did not improve following hemodialysis and treatment with high-dose steroids, pentoxifylline, and supportive therapy. The patient presented to the emergency department in severe metabolic acidosis with apH of 6.89. Our patient's course was consistent with the clinical course of methanol poisoning reported in the literature which correlates the severity of ocular changes to the degree of acidosis (6) and which suggests an initial pH of less than 7.2 is associated with a poor visual prognosis (7).

The role of early initiation of steroids remains controversial. As the toxicity from methanol optic neuropathy is mostly inflammatory, it has been hypothesized that high-dose steroids may help prevent blindness by inhibiting the demyelinating process.(4). Table 2 summarizes pertinent findings from the current literature exploring steroids and supportive management as potential treatments. In a previous case series, six patients treated within three days of methanol ingestion with 1 gram intravenous methylprednisolone daily for four days followed by 10 days of oral prednisone all experienced significant improvements in BCVA.(4). Of note, this report did not comment on the subjects' presenting pH. In a review evaluating 19 patients with pH levels varying from 6.47-7.30, Liu et al. found that patients who experienced a complete recovery had shorter durations of acidosis (8). In contrast, a review of 97 patients with pH levels between 6.82 and 7.37 concluded that early presentation did not seem to significantly alter the course of visual recovery (7). A case series published by Shukla et al. likewise found no significant relationship between time of treatment following poisoning and visual outcome among 17 patients presenting between 6 and 45 days following methanol ingestion (2). Notably, in addition to 1g methylprednisolone for 3 days followed by oral prednisone, these patients received one week of hydroxycobalamine as well as 6 weeks of cyclandelate and pentoxifylline, suggesting a potential benefit to supportive therapy as a supplement to steroid treatment.

Table 2: Summary of studies incorporating the use of corticosteroids in the management of acute alcohol toxic ingestion

Study	Design	Intervention	Inclusion Criteria (sample size)	Vision Related Outcomes	Select Results	Comments
Shukla M et al. (2006)[2]	Case series	• 1 gram IV methylprednisolone in 500 ml ringers lactate over 2 hours on days 1-3, then 40 mg of oral prednisolone for 14 day followed by a 4-6 week taper. • Oral cyclenelate (400 mg) once daily for 6 weeks. • IM hyroxycobalamine (1.5 ml) once daily for 1 week. • oral pentoxyphylline (400 mg) once daily for 6 weeks.	Sudden onset of blurred vision after alcohol intake, followed by severe loss of vision with semi-dilated or dilated pupil in most. (n = 17)	VA	• 1 Week: 10/17 patients showed improvement in VA by one Snellen's line. • 1 Month: 5 cases that did not show any visual recovery at 1 week showed gain in VA by one or more Snellen's lines. • 3 Months: 16/17 patients showed good visual recovery (1 previously improved case showed deterioration of VA).	-
Abrish ami M et al. (2011)[4]	Case series	• 250 mg IV methyl prednisolone every 6 h for 4 days, then 1 mg/kg of oral prednisolone for 10 days.	History of sudden visual loss following ingestion of homemade alcoholic beverages. (n = 6)	BCVA, optical coherent tomography of macula and optic nerve head, fundus photo, complete ophthalmologic exam of the patients.	Baseline: • Mean BCVA of 0.86±0.08 in the right eye and 0.93±0.1 in the left eye (using the logMAR scale). • Mean macular thickness (225.2 – 24.83 in the RE and 229.1 – 19.56 in the LE). • Optic disc swelling in 5 patients. • Nerve fiber layer edema in 4 patients. Following treatment: • Mean BCVA of 0.33±0.18 in the RE and 0.29±0.2 in LE. • Difference between baseline and after treatment BCVA (p=0.008 and p=0.003, respectively). Mean macular thickness and cup-to-disc ratio unchanged.	All males, mean age 26.34±2.7 years.
Khan P et al. (2013)[8]	Double-blind RCT	• Treatment group: oral pentoxifylline ≥6 weeks (16-18 mg/kg body weight given in two equal doses). • Control group: placebo for same duration. *Anti-glaucoma medications were given to all patients with glaucomatous optic atrophy*	Diagnosis of optic atrophy (from any cause) of less than one year duration. (n = 15 patients; 30 eyes)	BCVA, pupillary reaction, RAPD, fundus pictures.	• Treatment group: BCVA at baseline and 6 months were 1.35 ± 0.44 and 0.75 ± 0.45 (p=0.002). • Control group: BCVA at baseline and 6 months were 1.32 ± 0.42 and 1.31 ± 0.42 (p=0.157). • Treatment has no effect on RAPD and fundus pictures.	-
Chahal HS et al (2013)[9]	Case report	• 6 mg of dexamethasone, 400 mg of pentoxifylline and 400 IU of vitamin E, each given 3 times per day for 14 days, then dexamethasone tapered over 6 weeks. Pentoxifylline and vitamin E given for a total of 6 months.	Patient with radiation optic neuropathy following gamma knife therapy for partially resected pituitary tumour. (n = 1)	VA	• Baseline: counting fingers in the right eye, 20/20 in the left eye, RAPD. • 2 weeks: VA was 20/40 in the right eye, with marked improvement in the right visual field. • 6 weeks: 20/40 in the right eye, with further improvement in the visual field. • 18 weeks: 20/25 in the right eye.	-

Abbreviations: BCVA, Best Corrected Visual Acuity; NA, Not Applicable; RAPD, Relative Afferent Pupillary Defect; VA, Visual Acuity

Pentoxifylline is a phosphodiesterase inhibitor with rheologic action. It decreases the viscosity of the blood and improves microcirculation. It is hypothesized that pentoxifylline may augment axon regeneration following injury.(9). In addition to the findings of the aforementioned case series published by Shukla et al. (2), there exists a modest body of evidence supporting a potential therapeutic role for pentoxifylline therapy in treating a variety of optic nerve pathologies. For instance, in a small randomized control trial by Khan et al., treatment with pentoxifylline resulted in improved BCVA in cases of optic atrophy.(9) Additionally, Chahal et al. described a case reporting on potential benefits of pentoxifylline in radiation-induced optic neuropathy (10). While pentoxifylline in combination with steroids and supportive therapy was not beneficial in our case, further investigation is warranted.

In contrast to previous reports which demonstrate a potential benefit from the use of intravenous steroids, pentoxifylline and supportive therapy for methanol-induced optic neuropathy, the results of our case suggest limited benefit in patients with severe acidosis who do not present in a timely manner to a health care setting. Ultimately, the risks and benefits of these treatments must be evaluated on a case-by-case basis to decide what is best for each patient.

Declaration of interests

The authors have no potential conflicts of interests to disclose.

Patient consent

Consent for this case report was given by the patient on July 24th 2019.

References

1. Liesivuori J, Savolainen H. Methanol and formic acid toxicity: biochemical mechanisms. Pharmacol Toxicol. 1991 Sep;69(3):157-63.

2. Shukla M, Shikoh I, Saleem A. Intravenous methylprednisolone could salvage vision in methyl alcohol poisoning. Indian J Ophthalmol. 2006 Mar;54(1):68-9.

3. Sodhi PK, Goyal JL, Mehta DK. Methanol-induced optic neuropathy: treatment with intravenous high dose steroids. Int J Clin Pract. 2001 Nov;55(9):599-602.

4. Abrishami M, Khalifeh M, Shoayb M, Abrishami M. Therapeutic effects of high-dose intravenous prednisolone in methanol-induced toxic optic neuropathy. J Ocul Pharmacol Ther. 2011 Jun;27(3):261-3.

5. Nurieva O, Diblik P, Kuthan P, Sklenka P, Meliska M, Bydzovsky J, et al. Progressive Chronic Retinal Axonal Loss Following Acute Methanol-induced Optic Neuropathy: Four-Year Prospective Cohort Study. Am J Ophthalmol. 2018 Jul;191:100-115. doi: 10.1016/j.ajo.2018.04.015.

6. Shah S, Pandey V, Thakore N, Mehta I. Study of 63 cases of methyl alcohol poisoning (hooch tragedy in Ahmedabad). J Assoc Physicians India. 2012 May;60:34-6.

7. Desai T, Sudhalkar A, Vyas U, Khamar B. Methanol poisoning: predictors of visual outcomes. JAMA Ophthalmol. 2013 Mar;131(3):358-64.

8. Liu JJ, Daya MR, Carrasquillo O, Kales SN. Prognostic factors in patients with methanol poisoning. J Toxicol Clin Toxicol. 1998;36(3):175-81.

9. Khan P, Khan L, Awasthi U, Khan A, Siddique Z, Chand R. Pentoxifylline: A TherapeuticRemedy For Optic Neuropathies. J Evol Med Dent Sci 2013;20(2):3516–22.

10. Chahal HS, Lam A, Khaderi SK. Is pentoxifylline plus vitamin E an effective treatment for radiation-induced optic neuropathy? J Neuroophthalmol. 2013 Mar;33(1):91-3.

Author Biographies:

1. Keean Nanji is an ophthalmology resident at McMaster University

2. Alex Pozdnyakov is a graduate of McMaster University's school of medicine.

3. Dr. Teresa Semalulu is an internal medicine resident at McMaster University.

4. Dr. Ameen Patel is a general internal medicine staff physician at the Juravinski Hospital.