Journal of Clinical Toxicology
ISSN: 2161-0495

Gabay et al., J Clin Toxicol 2018, 8:2
DOI: 10.4172/2161-0495.1000379

Case Report Open Access

Reversal of Severe Methanol Induced Visual Impairment Due to Prompt Hemodialysis

Ohad Gabay[1*], Aviv Talmon[1], Erez Tsumi[2] and Carmi Bartal[3]

[1]*Department of Internal Medicine Resident, Soroka University Medical Center, Israel*

[2]*Department of Ophthalmologist, Soroka University Medical Center, Israel*

[3]*Department of Internal Medicine, Critical Care Medicine and Emergency Medicine Specialist, Soroka University Medical Center, Israel*

[*]**Corresponding author:** Ohad Gabay, Department of Internal Medicine Resident, Soroka University Medical Center, Beer Sheva, Israel, Tel: 972506965928; E-mail: ohadgab@clalit.org.il; ohadgab@gmail.com

Received date: April 15, 2018; **Accepted date:** April 25, 2018; **Published date:** May 04, 2018

Abstract

We report a case series of recovery from severe visual impairment due to methanol intoxication following treatment with fomepizol and prompt hemodialysis. Three adult males presented to our hospital few hours after unintended methanol intoxication. All patients reported weakness and dizziness, two of them suffered visual impairment with visual acuity loss and one of them presented complete blindness and unresponsive dilated pupils. Fundoscopy examination revealed edema of the disk margin. Their laboratory findings included severe high anion gap metabolic acidosis with elevated osmolar gap and methanol levels.

All three patients were treated with fomepizole, folic acid IV, and 2-3 sessions of hemodialysis four hours each. The first session of dialysis was performed about 16 h after the methanol ingestion. They all exhibited a full recovery including the patient with the blindness who reported normal vision 20/20 with normal fundoscopic examination on discharge at the fifth day of hospitalization.

This case report confirms the effectiveness of the combined treatment based on early dialysis with fomepizol in reversing the retinal impairment in methanol intoxication. The reversibility of retinal end organ damage demonstrated here raises doubts about the common thought regarding the poor outcome of methanol induced retinal end organ damage.

Keywords: Hemodialysis; Intoxication; Fundoscopy; Metabolism; Acidosis; Therapy

Introduction

Methanol poisoning is characterized by CNS depression, metabolic acidosis and visual changes. Most cases of methanol poisoning occur by ingestion and most contemporary exposure occurs from unintentional ingestion of windshield washer fluid and other automotive cleaning products. Without treatment the minimum lethal dose in humans is thought to be approximately 1 g/kg or 1.25 ml/kg which developed in less than an hour due to its rapidly absorption and rapid peak level creation after oral administration. Ocular manifestation of methanol toxicity is well characterized over the last century. Although methanol itself is nontoxic to the retina, its metabolite, formate is responsible for this toxicity [1,2]. The rate limiting step in the oxidation of methanol to formate depends on alcohol dehydrogenaze-(ADH) which convert methanol to formaldehyde. Aldehyde dehydrogenase creates formic acid from formaldehyde. Formate main mechanism of toxicity is its binding to cytochrome oxidase and blockade of oxidative phosphorylation which ended with anaerobic metabolism and development of lactic acidosis. In addition, the metabolism of methanol increases the $NADH/NAD^+$ ratio which favors the conversion of pyruvate to lactate and thereby worsens lactic acidosis.

The formate gradually accumulates in humans due to its folic acid elimination dependents and subsequent delayed toxic effect. After a latent period of 18 h patients classically develop central scotomata and blurred vision, as the toxicity progresses hyperemia of the optic nerve head and edema of the disc margin are seen on Fundoscopy [3,4]. These signs and symptoms may resolve with prompt treatment [5-7]. However continued formate accumulation results in more ominous signs of blindness, absent pupillary response to light, which considered irreversible and leads to permanent optic nerve atrophy [3]. The dose required to cause permanent visual impairment in an adult is estimated to be about a mouthful (24 g-30 ml).

The conventional treatment involves the administration of alcohol dehydrogenase inhibitor like ethanol or fomepizol (4-methylpyrazol) in order to block bioactivation of the parent alcohol to its toxic acid metabolites [5,8]. All methanol poisoning patients should also receive cofactor therapy with either leucovorin or folic acid to accelerate endogenous formate metabolism [5,9]. Acidemia makes the toxic metabolites to become uncharged molecules and more likely to penetrate end organ tissues like the retina. Thus treatment with sodium bicarbonate reduces end organ damage and improves the outcome [5,10]. The severity of poisoning correlates more with the level of acidosis than with the methanol level. The clinical signs and symptoms can develop in less than an hour but can be delayed for 24 h.

Indications for hemodialysis after methanol ingestion include: refractory metabolic acidosis PH<7.25 with anion gap >30 meq/L,

visual abnormalities, renal insufficiency, deteriorating vital signs despite aggressive care, electrolyte abnormalities refractory to conventional therapy and serum methanol level >50 mg/DL .

We report a case series of methanol intoxication in three men when one of them reported complete blindness on arrival and had a retinal edema in fundoscopy which is considered a sign of irreversible retinal damage, that due to prompt treatment mentioned above which included hemodialysis were discharged without any visual sequelae.

Case Report

Previously healthy three soldiers that served in international force in Sinai were brought to our hospital ten to twelve hours after drinking unknown substance for inebriation. The first patient presented with complete blindness, dizziness and weakness. The second complained on weakness dizziness without visual disturbance and the third patient presented with blurred vision dizziness and abdominal pain. A urine drug of abuse screen was negative. Their vital sign, symptoms and laboratory exams are summarized in Table 1.

	Patient 1	Patient 2	Patient 3
Vital signs			
Consciousness	+	+	+
Blood pressure	105/68	139/82	103/67
Pulse	94	65	84
Respiratory Rate	25	20	14
Saturation (room air)	94%	99%	95%
Laboratory exams			
PH	7.19	7.18	7.17
Anion gap	28	20	24
Osmotic gap	73	40	80
Methanol level	224	114	294
Urea (mg/dl)	46	27	26
Createnine (mg/dl)	1.46	1.3	1.21
Clinical presentation-complains and symptoms			
Blindness	+	-	-
Blurred vision	+	-	+
Pupilary light reflex	_	+	+
Dilated pupils	+	-	-
Dizziness	++	+	+
Severe weakness	++	+	++

Table 1: Clinical components and laboratory exams of the three patients.

Formal ophthalmologist assessment including a fundoscopy revealed edema of the disk margin and local hyperemia in the first patient, the fundoscopies of the other patients were normal. They all were treated with fomepizol 15 mg/kg in the emergency room 40 min after arrival, folic acid and sodium bicarbonate IV, after insertion of central lines, hemodialysis was initiated 2-3 h after arrival and actually 16-18 h after the methanol ingestion. At the completion of the first hemodialysis Methanol levels were 87, 51 and 169, PH levels were 7.45, 7.34 and 7.38 respectively, but we emphasize again that the patients were treated also with sodium bicarbonate IV. After 36-48 h and after performing two sessions of 4 h dialysis patient 1 and 3 reported visual disturbance improvement, patient 3 still had methanol levels of 72 mg/dl that decreased to 19 mg/dl only after the third session of dialysis (Figure 1).

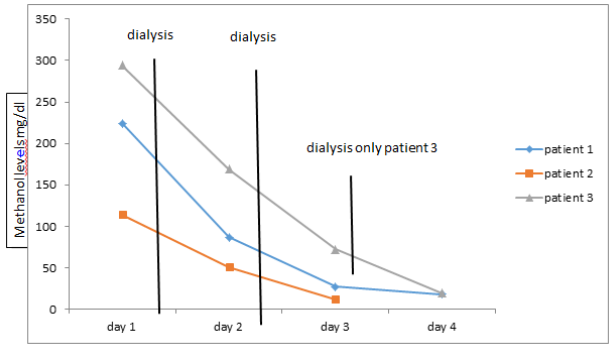

Figure 1: The Methanol levels (mg/DL) of three patients during hospitalization.

They all exhibited a full recovery with normal vision 20/20 and normal fundoscopy at discharge, including the first patient that presented full blindness.

Discussion

We presented three patients with severe methanol intoxication as evident by their laboratory exams and clinical manifestations. Two of the patients came with impaired visual acuity and one of them presented with retinal edema considered as an irreversible sign of retinal end organ intoxication damage [3].

We showed that prompt hemodialysis after methanol ingestion is efficient for end organ toxicity prevention and even in reversing of the retinal damage [11]. Decreasing methanol levels directly correlate with improvement and the complete resolution of the visual symptoms. Findings from this case also support the safety of Fomepizol which theoretically could potentiate methanol induced retinal toxicity by interfering with vitamin A metabolism as demonstrated in nonhuman primate data [12,13].

We challenged here one of the cardinal working premise in treating methanol intoxication saying that the severity of poisoning correlates more with the level of acidosis than with the methanol level. In our series, the clinical improvement was mainly correlated with methanol level decrease in blood although after the first dialysis session the patients had normal blood PH probably masked by sodium bicarbonate treatment. The importance of this case series is the proof that even severe retinal changes manifested with complete blindness may allow complete resolution of visual abnormalities after prompt treatment with fomepizole, hemodialysis, folic acid and sodium bicarbonate in the symptomatic methanol-poisoned patient.

References

1. Jacobsen D, McMartin KE (1997) Antidotes for Methanol and Ethylene Glycol Poisoning. J Toxicol Clin Toxicol 35: 127-143.
2. Martin-Amat G, McMartin KE, Hayreh SS, Hayreh MS, Tephly TR, et al. (1978) Methanol Poisoning: Ocular Toxicity Produced by Formate. Toxicol Appl Pharmacol 45: 201-208.
3. Benton CD Jr, Calhour EP Jr (1953) The Ocular Effects of Methyl Alcohol Poisoning: Report of a Catastrophe Involving 320 Persons. Am J Ophthalmol 36: 1677-1685.
4. Ingesmansson SO (1984) Clinical Observations on Ten Cases of Methanol Poisoning with Particular Reference to Ocular Manifestations. Acta Ophthalmol 62: 15-24.
5. Barceloux DG, Bond GR, Krenzelok EP, Cooper H, Vale JA, et al. (2002) American academy of Clinical Toxicology practice guidelines on the treatment of methanol poisoning. J Toxicol Clin Toxicol 40: 415-446.
6. Burns MJ, Graudins A, Aaron CK, McMartin K, Brent J, et al. (1997) Treatment of Methanol Poisoning with Intravenous 4-Methylpyrazole. Ann Emerg Med 30: 829-832.
7. Hantson P, Wallemacq P, Brau M, Vanbinst R, Haufroid V, et al. (1999) Two Cases of Acute Methanol Poisoning Partially Treated by Oral 4-Methylpyrazole. Intensive Care Med 25: 528-531.
8. Brent J, McMartin K, Phillips S, Aaron C, Kulig K, et al. (2001) Fomepizol for the treatment of methanol poisoning. N Engl J Med 344: 424-429.
9. Ghosh A, Boyd R (2003) Leucovorin (calcium folinate) in "antifreeze" poisoning. Emerg Med J 20: 466.
10. Paasma R, Hovda KE, Hassanian-Moghaddam H, Brahmi N, Afshari R, et al. (2012) Risk factors related to poor outcome after methanol poisoning and the relation between outcome and antidote—a multicenter study. Clin Toxicol (Phila) 50: 823-831.
11. Sivilotti ML, Burns MJ, Aaron CK, McMartin KE, Brent J, et al. (2001) Reversal of severe methanol-induced visual impairment: no evidence of retinal toxicity due to fomepizole. J Toxicol Clin Toxicol 39: 627-631.
12. Blomstrand R, Ingelmansson SO (1984) Studies on the Effect of 4-Methylpyrazole on Methanol Poisoning Using the Monkey as an Animal Model: With Particular Reference to the Ocular Toxicity. Drug Alcohol Depend 13: 343-355.
13. McMartin KE, Hedstrom KG, Tolf BR, Wintzell OH, Blomstrand R, et al. (1980) Studies on the Metabolic Interactions Between 4-Methylpyrazole and Methanol Using Monkey as an Animal Model. Arch Biochem Biophys 199: 606–614.