

**Instruction**

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## Methanol Toxic Optic Neuropathy: Clinical Characteristics and Visual Acuity Outcome after High-Dose Methylprednisolone

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Bandung, West Java, Indonesia**Abstract**

**Purpose:** To describe the clinical characteristics and visual acuity outcome in methanol toxic optic neuropathy patients after treatment with high-dose intravenous methylprednisolone.

**Method:** This is a descriptive retrospective study. Data were gathered from the medical records of 244 patients (488 eyes) diagnosed with methanol toxic optic neuropathy over a 5 year period (January 2010 until December 2014). They were treated with high-dose intravenous methylprednisolone 1 g/day followed by oral methylprednisolone 1 mg/kg which was tapered off. The sex, age, onset of blurred vision, time interval between alcohol ingestion and the treatment, funduscopic examination and visual acuity during the initial assessment, on the third day and at the one week, two week and one month follow-up visits were obtained and analyzed.

**Results:** There were 244 patients included in our study. Two-hundred-twenty six (92.6%) were male. One-hundred-six (43.5%) were 26–35 years of age. One-hundred-sixty-nine (68.3%) had onset of visual loss 24 hours after alcohol exposure. One-hundred-eighty-seven (64.5%) had an interval that was 2 days – 1 week between alcohol ingestion and steroid treatment. One-hundred-sixty-five (67.6%) had optic disc swelling seen by funduscopy. Most patients had an initial visual acuity between light perception and counting fingers at 1 meter. On the third day of intravenous methylprednisolone treatment, 288 out of 488 eyes (59%) showed improvement of visual acuity, 175 eyes (35.8%) showed no improvement and 25 eyes (5.1%) had decreased visual acuity.

**Conclusion:** The majority of patients were male and most cases were between the ages of 26–35 years of age. Loss of visual acuity mostly occurred after 24 hours of alcohol ingestion and the majority of cases received treatment 2 days–1 week of alcohol ingestion. Fundusopic examination showed optic disc swelling in most cases. Treatment with high-dose intravenous methylprednisolone may improve visual acuity of patients with methanol toxic neuropathy.

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**Key Words:** methanol toxic optic neuropathy, visual acuity, methylprednisolone

**Backgrounds**

Methanol intoxication remains a health problem in many parts of developing countries, especially among lower socioeconomic countries<sup>1,2)</sup>. There were

51 cases of methanol intoxication in Iran in 2000–2009<sup>3)</sup>. In West Bengal, India, an extraordinary incidence of 50 mortality caused by ingestion of methanol-containing alcohol, occurred over 3 days (May 3–6, 2009)<sup>4)</sup>. In America, the incidence of

group. There were 169 out of 244 cases that were found in the 26 to 35-year-old age group (43.5%). The highest numbers of cases (106 out of 244 cases patients). Most of the patients were male (92.6%). **Table 1** shows the clinical characteristics of the every year during the five-year period (**Figure 1**).

During January 2010–December 2014, there were 244 patients or 488 eyes with methanol toxic optic neuropathy. The number of case per year increased every year during the five-year period (**Figure 1**).

## Results

Ciencio Eye Hospital from October to December 2015. The study was conducted at the National Eye Center Office Excel 2007 and shown in tables and figures. Data was analyzed descriptively using Microsoft

improvement, and decreased. outcome was categorized into improvement, no divided into 6 categories of visual impairment based on the WHO working definition<sup>11</sup>. Visual acuity was divided into 1 month, 1 week, 2 weeks, and 1 month. Visual acuity was at the initial assessment, on 3 day and at the 1 copic evaluation at first visit as well as visual acuity methanol consumption and initial treatment, fundus examination after alcohol ingestion, interval between visitation that were collected including onset of decreased including sex and age. The clinical characteristics 2014. The demographic data that were obtained at Ciencio Eye Hospital, from January 1, 2010 to December 31, at 1 mg/kg at the National Eye Centre Ciencio Eye a gradual taper of oral methyldenisolone starting prednisolone (4x250 mg/day for 3 days), followed by which was treated with intravenous methyldenisolone which was treated with optic neuropathy patients with methanol toxic optic neuropathy was retrospectively obtained from medical records of This was a descriptive observational study. Data

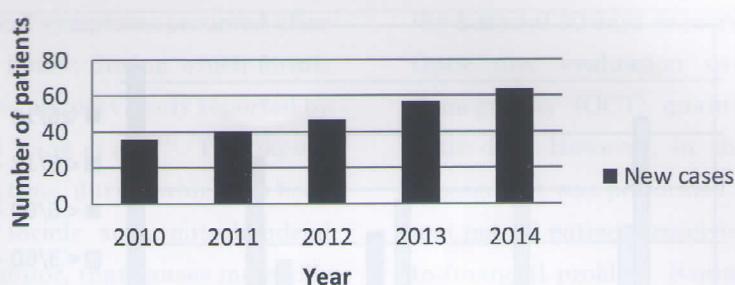
## Materials and Methods

evaluating the effect of high dose intravenous methanol toxicity was approximately 1,000–2,000 cases each year, yet that was only 1% of all toxicity cases<sup>5</sup>. Methanol ingestion causes severe visual failure such as permanent blindness or even death<sup>6</sup>. Methanol, well known as wood alcohol, is a solvent compound commonly used as glass cleaner, photocopy liquid, paint removal, perfume, and octane additive for gasoline. Methanol toxicity occurs as a result of ingesting alcoholic beverages that are illegally mixed with methanol, or suicide attempt by consuming compounds containing methanol. Methanol can also be absorbed into the body by inhalation or skin contact<sup>1,2,6</sup>.

further damage to the optic nerve<sup>10</sup>. Studies loss and intravenous steroid are used to avoid edema is considered a target for prevention of visual edema pathway worsens the damage<sup>10</sup>. Therefore, nerve fibers<sup>7</sup>. Elevated pressure due to edema in the develop edema that generates compress and suppres sensitive to methanol toxicity<sup>6,9,10</sup>. Damage myelin that myelin of the retrolaminar optic nerve is of formic acid<sup>6–8</sup>. A histopathologic study reports competitive inhibitor to prevent the generation of formaldehyde. Hemodialysis increases the elimination of methanol. Ethanol or formic acid is given as cramps, and coma) which are due to toxic complications, such as metabolic acidosis, threatens condition (such as metabolic acidosis, consists of evaluation and correction of life-management of methanol toxic optic neuropathy ble for ocular toxicity<sup>1–6</sup>.

which generate formic acid. Formic acid is responsible for methanol by formaldehyde dehydrogenase and generate formaldehyde. Formaldehyde is further metabolized by alcohol dehydrogenase. Methanol is metabolized by alcohol dehydrogenase disease, are commonly found in later stages<sup>6,7</sup>. midal syndrome similar to that seen in Parkinson's disease, coma, metabolic acidosis, and extrapyramidal symptoms, such as copic upon awakening. Clinical symptoms such as copic, visual impairment is usually the only symptom, visual impairment is after methanol consumption upon awakening. During the latent phase (12–24 hours after methanol consumption), visual impairment to medium toxicity. During the euphoria from light to medium toxicity. During the vomiting, abdominal pain, headache, vertigo, and gastrointestinal system. Symptoms include nausea, volves the central nervous system, eyes, and clinical manifestation of methanol toxicity in inhalation or skin contact<sup>1,2,6</sup>.

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**Figure 1.** Incidence of Methanol Optic Neuropathy in 2010–2014

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**Table 1.** Characteristics in patients with methanol optic neuropathy

Characteristics	N = 244	Percentage
<b>Sex</b>		
Male	226	92.6
Female	18	7.4
<b>Age</b>		
<15	0	0
15-25	78	31.9
26-35	106	43.5
36-45	46	18.9
>45	14	5.7
Onset of visual loss after drinking adulterated alcohol		
≤ 24 hour	75	30.7
>24 hour	169	68.3
Interval between drinking adulterated alcohol and steroid treatment		
≤24 hour	18	6.3
2 days-1 week	187	64.5
>1 week-4 week	77	26.7
>1 month	6	2.5
Funduscopic examination		
Normal optic disc	69	28.2
Swelling optic disc	165	67.6
Atrophy optic disc	10	4.2

experienced visual loss 24 hours after alcohol exposure. Interval between ingesting alcohol and initiation of steroid treatment in 187 patients (64.5%) was between 2 days and 1 week. Funduscopic examination during the initial assessment was normal in 69 eyes (28.2%). Optic disc atrophy was seen in 10 eyes (4.2%), and optic disc swelling in 165 eyes (67.6%).

On initial assessment, most patients had visual acuity between light perception and counting fingers at 1 meter. This occurred until the 1-week follow up,

although the number of patients in this visual acuity category decreased gradually. The number of patients who were lost to follow-up started to increase after the 1-week follow-up (**Figure 2**). Therefore, the visual acuity outcome can only be assessed on third day of intravenous methylprednisolone treatment.

Visual acuity outcome on the third day of intravenous methylprednisolone was improved in 288 eyes (59%). There was no improvement in 175 eyes (35.8%), and decreased visual acuity in 25

## Discussion

eyes (5.12%) (Table 2).

Methanol metabolism of methanol into its toxic metabolite, formaldehyde, is an antidiote to inhibit the metabolic acidosis and an antidiote to correct the buffer, such as sodium bicarbonate, to correct the management of metabolic acidosis consists of a solution creates the toxicity of methanol.

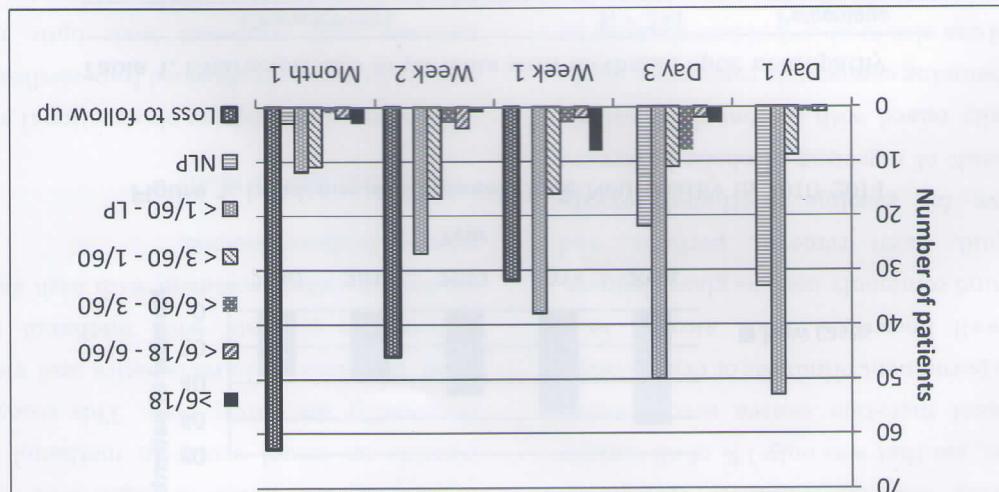
and the intrinsic toxicity of the formate (formic acid) and the anion and osmolar gap<sup>7,9</sup>. The combined effect of metabolic acidosis ( $H^+$  production) and the anion and osmolar gap<sup>7,9</sup>. The acidosis and the anion gap<sup>7,9</sup>. The clearance<sup>6,14</sup>. Formic acid is responsible for metabolic clearance<sup>6,14</sup>. Formic acid causes its accumulation to exceed its hours), which causes it slowly metabolized (20 hours). Formic acid is slowly metabolized (20 detectable in bodily fluid after ingesting toxic dose of methanol. Formic acid is formed after ingesting toxic dose of its rapid metabolism (1-2 minutes) makes it unstable in body. Although formaldehyde is toxic, it is further metabolized by formaldehyde dehydrogenase. When methanol is metabolized by alcohol dehydrogenase, formaldehyde is formed. Formaldehyde drogogenase, formaldehyde is formed. Formaldehyde is further metabolized by formaldehyde dehydrogenase.

When methanol is metabolized by alcohol dehydrogenase, formaldehyde is formed. Formaldehyde is further metabolized by formaldehyde dehydrogenase.

Visual Acuity	N = 488	Percentage	
Decreased	5.1	25	No Improvement
Improved	59.0	288	Improvement
NILP	35.8	175	No Improvement

Table 2. Visual acuity outcome on third day of intravenous methyldnisolone treatment.

Figure 2. Visual acuity in methanol toxic optic neuropathy after intravenous



where the onset of clinical symptoms occurred after a latent period (12–24 hour), during which formic acid is at its highest level are previously reported by Stelmach *et al.* and CS Yang *et al*<sup>10,15</sup>. This occurs due to the need for a lag time, during which the body metabolizes the toxin formic acid, mitochondrial cytochrome oxidase inhibitor, that causes metabolic acidosis<sup>16</sup>.

Ocular problems emerge due to the effects of methanol toxicity on the oligodendrocyte axon of the retrolaminar optic nerve<sup>15</sup>. Its pathogenesis occurs through the binding between formic acid and cytochrome oxidase in the respiratory chain of the mitochondria leading to histotoxic hypoxia. This causes the inhibition of mitochondrial function and the reduction of ATP synthesis in the retina and optic nerve. Low levels of ATP reduces the activity of the Na<sup>+</sup>, K<sup>+</sup> ATPase-pump inhibiting the creation of a membrane potential and thus nerve conduction, damaged myelin, and visual impairment<sup>6</sup>. Moreover, axoplasmic current stasis caused intra-axonal and optic disc swelling. Damaged myelin become edematous generating compression or suppression of nerve fibers<sup>6</sup>. Sharpe *et al.* reported on the damaged myelin of retrolaminar optical neurons from post mortem histopathologic examination of 4 methanol toxicity cases.

Fundoscopic examination in acute methanol intoxication demonstrate optic disc hyperemia and swelling that occur simultaneously with the onset of visual impairment<sup>6,15–18</sup>. Optic disc swelling was found in 165 cases (67.6%) in this study. Abrishami *et al.* reported that 66.6% of methanol optic neuropathy cases came with optic disc swelling<sup>19</sup>. Peripapillary retinal edema slowly occurred and lasted for two weeks, followed by occasional retinal vein dilatation<sup>6,15,17</sup>. Mitochondrial disruption causes histotoxic anoxia which results in the optic disc hyperemia or edema seen on the initial fundoscopic assessment with associated blurred vision. If uncorrected, this can progress to optic atrophy<sup>16</sup>.

Optic disc atrophy developed in 30–60 days<sup>15,18</sup>. In this study, optic disc atrophy occurred in 10 eyes (4.2%), even though six patients (12 eyes) visited

the hospital 30 days or more after alcohol ingestion. Optic disc evaluation using Optical Coherence Tomography (OCT) quantitatively measure the optic disc. However, in this study the optic disc assessment was performed using direct funduscopy and not all patients received OCT examination due to financial problem. Samantha *et al.* report 100% optic disc atrophy in 10 methanol toxic optic neuropathy patients, who were all chronic alcoholic for more than 10 years<sup>4</sup>. It may be concluded that a long-term history of alcohol consumption causes optic disc atrophy. In this study, the history of alcohol consumption was not obtained.

A normal optic disc was found in 69 cases (28.2%) in this study. Sharpe *et al.* also report that 3 out of 4 patients with methanol optic neuropathy had normal optic discs. Post-mortem histopathology analysis of four patients from a previous study was performed and demyelination was found on the retrolaminar optic nerve<sup>9</sup>. The selective sensitivity on the retrolaminar optic nerve in methanol toxic remains unclear. However, there is an overlapping arterial circulatory pattern and a “watershed effect” theory that created high concentration formic acid in that area has been proposed<sup>9,10,13</sup>. High levels of choriocapillary blood flow, small amount of mitochondria, and low levels of cytochrome oxidase in the nerve fibers of the retrolaminar optic nerve and its myelin could be predisposing factors for the selective sensitivity of the retrolaminar optic nerve in formic acid histotoxic hypoxia effects<sup>6,7</sup>.

Visual acuity outcome in this study was assessed on day 3 of intravenous methylprednisolone treatment due to the increasing number of patients who were lost to follow-up at the 1-week, 2-week, and 1 month follow-up visits. Improvement in visual acuity occurred in 59% patients. Shukla *et al.* report improvement in visual acuity in 88.2% cases, 3 months after treatment with intravenous methylprednisolone<sup>20</sup>. Abrishami *et al.* report that 6 cases of methanol toxicity treated by intravenous methylprednisolone resulted in significant improvement 3 months after treatment<sup>19</sup>. Sodhi *et al.* report improvement in visual acuity in 4 cases of methanol toxic optic neuropathy after treatment with high-

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### **Conclusion**

The amount of methanol consumed, concentration of methanol at admission, the duration of the latent period, interval between methanol consumption and treatment, and metabolic acidosis were factors affecting visual impairment<sup>2,6</sup>. The interval between alcohol ingestion and treatment in this study was 2 days (61.7%), the interval was 2 days -1 week. Mangunkuya et al. report an interval > 12 hours between methanol consumption and treatment correlated with the morbidity level (visual impairment) and mortality<sup>2</sup>. However, Rotenstreich et al. report that improvement in visual acuity in methanol toxic neuropathy occurred after 10 days of treatment<sup>24</sup>. The absence of data regarding the amount of methanol consumed and serum concentration of methanol in our study may be a limitation of this study.

This study did not compare the treatment group of patients with a control group due to methyldiphenylisobutylamine being included as the standard therapy for methanol toxic optic neuropathy at the Cincinnati Eye Hospital. Patients with optic neuropathy who have been informed about a poor prognosis still demand treatment. Therefore, some patients with optic neuropathy received methylprednisolone treatment.

dose intravenous steroid<sup>21</sup>.

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