Methanol Poisoning: Our Experience with Recent Outbreak

Reema Rajbhandari, MBBS
Department of Medicine
Tribhuvan UniversityTeaching Hospital
Kathmandu, Nepal

Dr Niranjan Acharya, MD
Department of Medicine
Tribhuvan UniversityTeaching Hospital
Kathmandu, Nepal

Prof J P Agrawal MD
Department of Medicine
Tribhuvan UniversityTeaching Hospital
Kathmandu, Nepal

Address for correspondence
Reema Rajbhandari, MD
Department of Medicine
Tribhuvan UniversityTeaching Hospital
Kathmandu, Nepal
Email: reemarajbhandari@hotmail.com

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Alcoholic drinks adulterated with methanol may result in metabolic acidosis, blindness, and death. Inhibition of alcohol dehydrogenase is the fundamental in the treatment of methanol poisoning. Recently there was an outbreak of methanol poisoning in Sindhupalchowk and Sindhuli in Shrawan, 2065 BS (July- August, 2008 AD). Seven cases presented to Tribhuvan University Teaching Hospital with acute visual impairment and other neurological problems. Active management with high dose intravenous steroid and other accessory modalities was carried out. Vision of only 2 cases improved and others' didn't. Other helpful modes of treatment are fomepizole, folate, hemodialysis etc. Health workers and general public should be well educated about health hazard of local alcoholic drinks to prevent methanol poisoning. Strict legal forces with proper rules and regulation should be implemented. By this, many lives and vision of victims can be saved.

Key Words: folate, fomepizole, hemodialysis, methanol.

Recently there had been an outbreak of methanol poi soning in Shrawan, 2065 BS (July- August, 2008 AD) in Sindhupalchok and Sindhuli districts of Eastern Nepal. Investigations done by Nepal Academy of Science and Technology (NAST) with the samples obtained from the epidemic area showed that "Sofi", a locally brewed alcoholic drink, was adulterated with methanol leading to death of seven people in Sindhupalchok and three in Sindhuli. Methanol is a highly toxic substance and acute methanol poisoning produces severe metabolic acidosis and serious neurological symptoms, including acute and severe visual impairment, extrapyramidal signs and finally coma. The lethal dose of pure methanol is estimated to be 1-2 mL/kg; however, permanent blindness and death have been reported with as little as 0.1 mL/kg[5]. Its similarity to ethanol in appearance and odor promotes illegal trade. Seven cases of methanol poisoning from epidemic area were admitted with acute visual deficit in Tribhuvan University Teaching Hospital (TUTH). Four cases were admitted in the department of medicine, neurology unit and three were in ophthalmology. Here we report briefly about the presentation, treatment and outcome of four cases admitted in the Neurology unit Department of Medicineand discuss overall aspects of methanol poisoning.

Cases

Case Number 1

A 46-year-old male, smoker and occasional drinker, from Sindhupalchok ward no. 3 complained of headache, vomiting and bilateral painless loss of vision over a period of two hours after drinking "Sofi" followed by loss of consciousness (LOC) for 2-3 hours, dysphagia while taking liquid, nasal regurgitation, and mild cough. He was treated in local District hospital initially and was referred to TUTH for further management. On examination blood pressure (BP) was 160/90 mm Hg., Glasgow Coma scale (GCS) was 14/15, tone increased on all four limbs, bilateral (BL) pupils were 3-4mm and round. Direct as well as consensual pupillary light reflexes were sluggish in the right eye where as in the left eye direct light reflex was sluggish but consensual light reflex was normal. Funduscopic examination revealed BL papilloedema **(Figure 1)**. ABG analysis showed normal probably because of late presentation

Case Number 2

A 50-year-old female, from Sindhupalchok ward no. 4 also complained of headache vomiting and bilateral painless loss of vision after drinking "Sofi". She developed LOC, urinary and fecal incontinence with generalized weakness and was treated in district hospital with Amlodipine 5mg for hypertension and referred to TUTH. On examination her BP was 110/70 mm Hg. Neurological examination showed GCS 11/15 tones increased on all four limbs, BL pupils were 3mm and round. Direct and consensual pupillary light reflexes were sluggish bilaterally with BL optic disc hyperemia **(Figure 2)**.

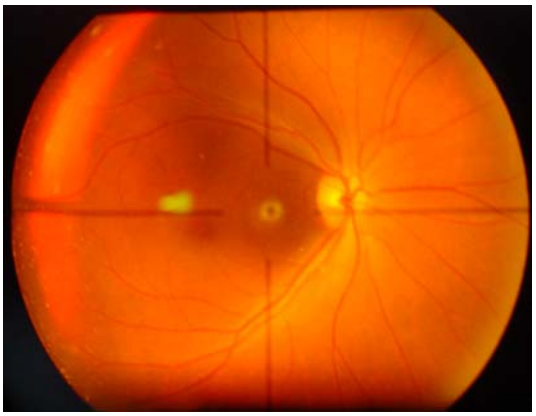

Figure1. Picture of right fundus of case no. 1 showing hyperemic fundus suggesting papilloedema

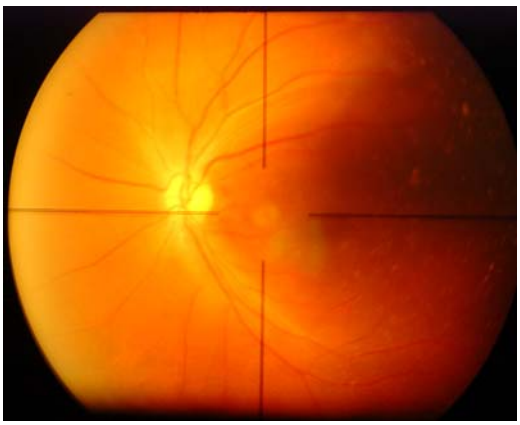

Figure2. Picture of left fundus of case no. 2 showing pale optic disc suggesting atrophy

Case Number 3

A 51-year-old male, from Sindhuli came with complaints of decreased vision, epigastric pain and LOC after taking local alcoholic drink. On examination, BP was 100/70 mm Hg. Neurological examination showed GCS 10/15 BL pupils were 4mm, fixed and nonreacting to light. Fundus examination showed BL optic atrophy. On arterial blood gas (ABG) analysis, pH was 7.2, pCO^2 was 126, pO^2 was165, HCO^3 was 6.1mmol/ L and SpO^2 99.4%.

Case number 4

A 46-year-old male from Sindhuli came with complaints of BL sudden painless loss of vision and headache for 1 day. On examination, BP was 110/80 mm Hg. Neurological examination showed GCS 15/15, BL pupils were 4mm, fixed, nonreacting to light and with no perception of light. Fundoscopic examination showed signs of papilloedema. On ABG analysis, pH was 7.225, pCO^2 was 14.5, pO2 was 100 and SpO^2 was 96.7%. On repeat ABG analysis next day, pH was 7.4, pCO^2 was 22, pO^2 was 81.3, and SpO^2 was 90%.

Apart from these four cases, there were other three cases admitted from the same district in the Ophthalmology department with similar history of painless loss of vision, headache and vomiting. First two cases had no perception of light in both eyes and third had perception of light in right eye and hand movement in left eye after treatment.CT scan of head in all the 4 cases showed hypodense area in BL basal ganglia region mainly lenticular nucleus suggesting infarction **(Figure 3)**.

Treatment

Treatment with high dose intravenous injection of steroid i.e. Methylprednisolone 1gm was given for 3 days with other supportive treatment, Ethanol, Follinic acid was used, Injection Sodium bicarbonate was given and acidosis was corrected. Case 3 got additional treatment with Hemodialysis twice. Fomepizole could not be used for any of the patients, as it was not available.

Outcome

The vision of case no. 1 improved from complete blindness to finger counting and that of case no. 2 improved from complete blindness to 6/12 on right eye and 6/18 on left eye. However, the vision of case no. 3 and 4 remained nonperception of light BL. All the patients improved neurologically to some extent.

Discussion

Methanol is converted to formaldehyde by alcohol dehydrogenase then to formic acid by aldehyde dehydrogenase, which is then degraded to carbon dioxide (CO2) and water, where folate is a cofactor. In this reaction, formic acid causes metabolic acidosis and CNS damage. The production of formic acid takes time which explains the delay in the onset of the symptoms[9]. It inhibits cytochrome oxidase in the fundus of the eye causing disruption of the axoplasm due to impaired mitochondrial function and decreased ATP production. Swelling of axons in the optic disc leads to visual impairment.[8]

Visual disturbances, including decreased visual acuity, photophobia, and blurred vision, and abdominal pain are the most common symptoms of methanol intoxication.[2] Hyperemia of the optic discs and reduced pupillary response to light may be present.Case1,case 2, and case 4 developed papiloedema and case 3 developed optic atrophy of both eyes.Although most patients recover to normal visual function, permanent impairment of vision may occur. In the case 1 and 2 vision improved but case 3 and case 4 developed complete blindness this may correlate with the amount of intoxication by methanol.Abdominal pain can be present in both the presence and absence of pancreatitis. Neurologic abnormalities including confusion, stupor, and coma are often present. A rare complication of methanol intoxication is putaminal necrosis, which presents with rigidity, tremor, masked faces, and monotonous speech. It has been attributed to the reduced cerebral blood flow and/ or accumulation of formic acid in the putamen.[4] The cases that we presented also showed basal ganglia infarction though not typical putaminal necrosis. Although the syndrome often resolves, some neurologic abnormalities can persist. Visual and neurological deficit is directly correlated with the severity of the metabolic acidosis. Kusmaul's breathing, impaired cardiac function, and hypotension as a result of acidemia can be present and are most profound when blood pH is below 7.2. Measurement

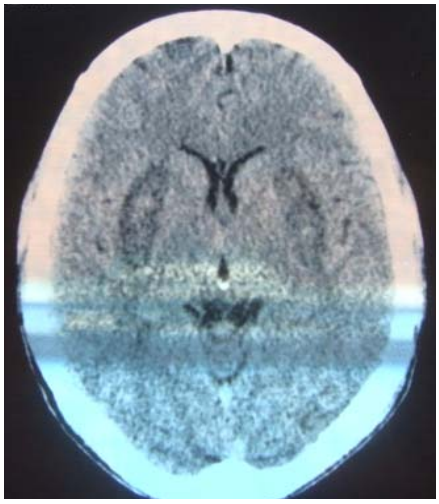

Figure 3. Computed tomography of case no 2 showing hypodensity in bilateral lentiform nucleus suggesting infacrtion.

of methanol in blood is important to confirm the diagnosis of methanol intoxication and can be valuable in assessing the response to treatment. As noted previously, in the absence of measurements of serum methanol, assessment of changes of the serum osmolal gap can be useful in some cases, for both the diagnosis and assessment of methanol intoxication.

The serum osmolality can be increased or normal. In patients who also consumed ethanol, ketoacidosis can occur. The ratio of AG with HCO_3^- (AG/HCO_3^-) may be >1 in some patients, reflecting either a concomitant metabolic alkalosis or a difference in the space of distribution of formate and HCO3. The serum anion gap may be minimally increased and serum $HCO3^-$ minimally reduced early in the course of the disorder, a time when the increment in serum osmolality is the greatest. Subsequently, as methanol metabolism proceeds, the serum HCO3– falls concomitantly with a rise in the anion gap and fall in the serum osmolality. After the bulk of the methanol has been metabolized, little or no increase in serum osmolality will be present, whereas the serum anion gap can be strikingly increased and the serum HCO3– markedly depressed. In rare instances, patients may have ocular toxicity in the presence of normal serum osmolal and anion gaps. Correct determination of serum creatinine can be obtained using an enzyme-based assay.[6]

Basic primary and supportive care and gastric lavage, if seen in first few hours, is helpful. Prevention of metabolism of methanol can be obtained by Ethanol and Fomepizole.[1,2,3] Formic acid excretion can be enhanced by Folate given 1mg/ kg intravenously every 4 hourly. Correction of acidosis by sodium bicarbonate and lastly removal of methanol by dialysis are the specific measures.[7] Indications for dialysis include ingestion of more than 30 ml of methanol ingested, serum methanol level greater than 20 mg/ dl, presence of visual complications, and no improvement of acidosis despite repeated sodium bicarbonate infusions.[6]

The case that we presented had optic and neurological manifestations. Among them one had developed severe metabolic acidosis and the rest had already recovered from acidosis.In all four cases the neurological manifestation remains the same because of bilateral lenticular lesion.

Conclusion

Diagnosis of methanol poisoning is often delayed dueto lack of coordination between local people and healthmanpower and delay in investigation by expert team.Almost 10 people from Sindhupalchok and Sindhulidied and many more had permanent visual impairment. Despite knowing about the complications of methanol, we have not been able to educate the local people. Because of the ignorance of rural people and the ineffective support from government, uncontrolled adulteration is rampantly leading many people to lose their vision and lives

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