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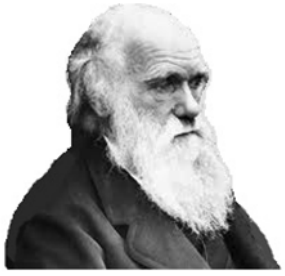

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Methyl Alcohol Poisoning

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ABSTRACT

Methyl alcohol is a cheap and potent adulterant of illicit liquors. Many outbreaks of methyl alcohol poisoning have occurred in our country. Such outbreaks have been responsible for a heavy toll of mortality and morbidity. This paper describes our clinical experience in managing patients with methyl alcohol poisoning, and emphasizes that early identification and prompt treatment is of prime importance. Methanol, also known as wood alcohol, is a commonly used organic solvent that, because of its toxicity, can cause metabolic acidosis, neurologic sequelae, and even death, when ingested. It is a constituent of many commercially available industrial solvents and of poorly adulterated alcoholic beverages. Methanol toxicity remains a common problem in many parts of the developing world, especially among members of lower socioeconomic classes (See Etiology and Pathophysiology and Presentation).

***Keywords*:** Methyl alcohol, poisoning

1. INTRODUCTION

A 30 years old male, labourer and moderate drinker was admitted to our hospital with history of acute loss of vision after consumption of toxic alcohol 3 days earlier. The patient was found to have consumed about 200 ml of illicit alcohol “moorie”, allegedly adulterated with paint thinner, with two of his other labourer friends in a remote area. Both of his victim friends died within 1-2 hours and the patient also started having vomiting, headache, confusion, and diminution of vision within 2-3 hours of consumption of toxic alcohol. The patient was treated at local hospital with supportive therapy and referred to us after a delay of 3 days.

On examination the patient revealed blood pressure of 120/80 mm of Hg, pulse rate of 90/ min, respiratory rate of 24/min, drowsiness with Glasgow Coma Scale of 14/15 and normal systemic examination. Bilateral ocular examination revealed dilated pupils, sluggish reaction to direct and consensual light reflexes, absence of perception of light and resolving papilledema on ophthalmoscopy.

Laboratory investigations revealed normal blood count, blood sugar, renal and hepatic parameters. Arterial blood gas (ABG) analysis revealed metabolic acidosis with pH - 7.216, p CO_2 - 15.8 mm Hg, HCO_3^- - 6.3 meq/L, Na^+ - 146 meq/L, K^+ - 4.1 meq/L and Cl^- - 110.7 meq/L and elevated anion gap of 29. However the blood methyl alcohol level could not be estimated in the absence of laboratory facilities. Non contrast CT Head revealed hypodense lesions with hyperdense specks in bilateral lentifrom nuclei. In view of suspicion of illicit toxic alcohol ingestion, acute visual loss and metabolic acidosis with high anion gap, the clinical diagnosis of methyl alcohol poisoning was entertained, which met the diagnostic criteria (Table 1).

Accordingly, the patient was managed aggressively with sodium bicarbonate (10%) 100 ml, administered intravenously every two hourly, oral ethyl alcohol (42.8%) 120 ml, given as loading dose followed by 18 ml hourly maintenance dose, titrated to 30-35 ml hourly for hemodialysis,following dosage regimens (Table 2), and oral folic acid 50 mg four hourly. Intravenous methyl prednisolone 1 gm for 3 days followed by 60 mg oral prednisolone was given to salvage vision. The patient showed improvement in metabolic acidosis and the treatment with sodabicarbonate, oral ethyl alcohol and hemodialysis was continued for three days until pH >7.35 as revealed by ABG analysis, pH – 7.45, HCO_3^- 24.3 meq/L and anion gap of 9. But the patient revealed no visual improvement.

The repeat bilateral ophthalmic examination revealed no perception of light, optic atrophy on fundoscopy (Figure 1a and b) and fundal ischemic changes on fundus fluorescence angiography. Non-contrast CT head, T1-weighted and FLAIR MR images of brain (Figures 2a,b and 3a) revealed bilateral putaminal hemorrhagic necrosis consistent with characteristic findings of selective neurotoxicity of methyl alcohol. FLAIR MR image of brain also revealed linear hyperintensities in intraorbital parts of bilateral optic nerves suggesting optic nerve damage (Figure 3b). The patient improved with aggressive treatment however, the occurrence of permanent blindness could not be prevented probably because of late presentation. Patient was discharged with advice to follow up.

Table 1. Criteria of diagnosing methanol toxicity

1. Documented plasma methanol concentration	> 20 mg/dL (> 200 mg/L).
2. Documented recent history of ingesting toxic amounts of methanol and osmolal gap	> 10 m Osm/kg.
3. History or strong clinical suspicion of methanol poisoning with at least two of the following criteria:	
a. Severe metabolic acidosis i.e. Arterial	pH < 7.3
b. Serum bicarbonate	< 20 meq/L (mmol/L)
c. Osmolal gap	> 10 m Osm/kg

Table 2. Ethanol dosage regimens

A. Loading Dose of Ethanol	
1. Intravenous:	7.6 – 10 mL/kg of a 10% solution in Dextrose 5%. Ethanol is available as 5% or 10% solutions in Dextrose 5%; the latter is preferred.
2. Oral:	0.8 – 1 mL/kg of 95% Ethanol, administered PO in orange juice.
B. Maintenance Dose of Ethanol	-

Fig. 1 a and b. Right (a) and left (b) fundal pictures showing pale optic discs with extending atrophic changes to retinal nerve fibers layers suggesting optic atrophy.

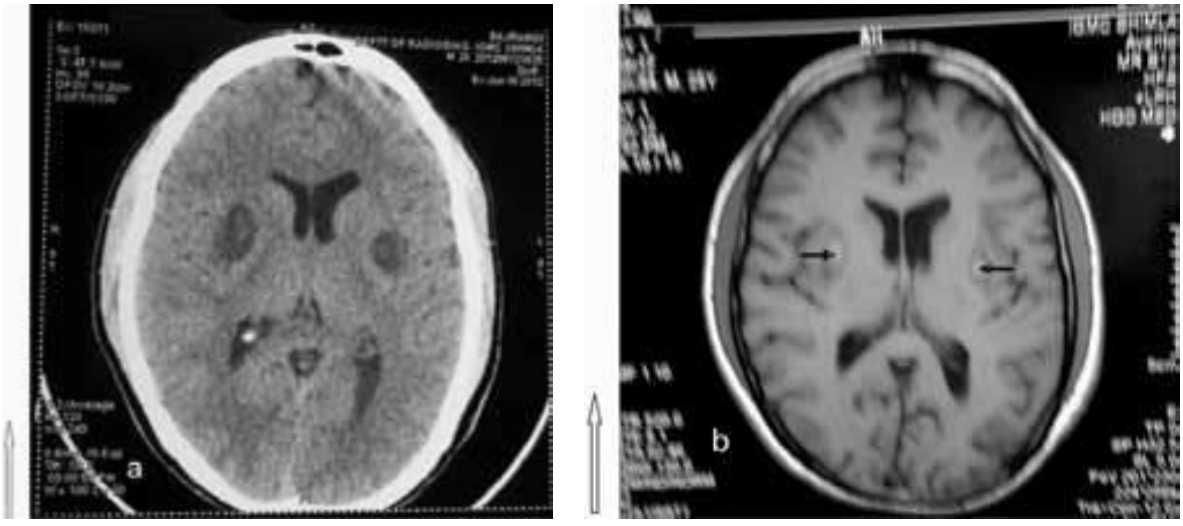

Fig. 2 a and b. Non contrast axial CT head (a) showing hypodense areas involving bilateral lentiform nuclei with hyperdense specks within and T1 – weighted axial MR image of brain showing hypointense lesions with central hyperintensities (*arrows*) in putamina, suggesting bilateral putaminal hemorrhagic necrosis.

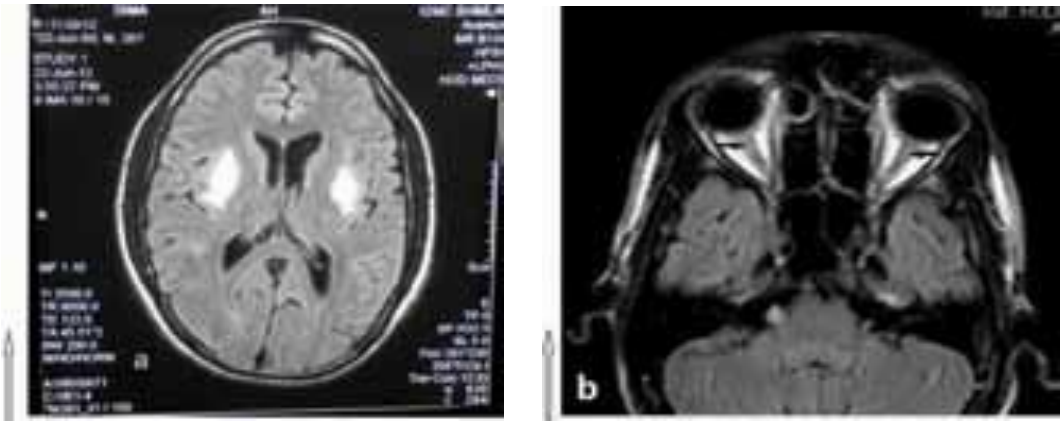

Fig. 3 a and b. Axial FLAIR MR images of brain (a) showing hyperintensities suggesting bilateral putaminal hemorrhagic necrosis and linear hyperintensities (*arrows)* in intraorbital parts of bilateral optic nerves (*mlagnified view*, b) suggesting atrophy

2. DISCUSSION

Methyl alcohol or methanol (CH_3OH) or wood alcohol, is a colorless, volatile and toxic liquid having specific gravity of 0.81, boiling point of 650 °C and molecular weight of 32.04 g $mole^{-1}$. It is found frequently in high concentration in automotive antifreeze, de-icing solutions, windshield wiper fluid, varnishes, paint thinner and many other industrial products. Methyl alcohol poisoning most commonly occurs via oral ingestion of illicit or adulterated liquors or as ethanol substitution, also absorbed transdermally or by inhalation. Reports of outbreak of methyl alcohol poisoning from different parts of India revealed that the victims are poor people in rural areas with lack of infrastructures and tertiary care facilities resulting in high mortility [1-4].

Methanol kinetics ensue and lead to profound toxicity following ingestion of large dosages of toxic alcohol. Methyl alcohol is rapidly and completely absorbed after oral ingestion, peak serum concentration reaches within 30 to 60 minutes. The lethal dose is 30-50 ml, the smallest reported to cause death is 15 ml of 40% of methyl alcohol. The permanent blindness may occur with the dose as little as 10 ml. The latency period is 12 to 36 hours which is peculiarity of methanol poisoning. Methanol is oxidized by hepatic metabolism to formaldehyde and formic acid facilitated by alcohol dehydrogenase (ADH) and aldehyde dehydrogenase (ALDH) respectively and ultimately to its end products, the water (H_2O) and carbon dioxide (CO_2).

Hepatic elimination of methanol follows zero- order kinetics and have elimination half life of 14 to 18 hours without treatment. If hepatic oxidation is inhibited by alcohol dehydrogenase antagonists such as ethanol and fomepizole, the methanol elimination shifts to the pulmonary and renal routes, becomes first - order kinetics and slows dramatically to an elimination half life of 48 to 54 hours. Methanol toxicity occurs as a result accumulation of toxic metabolite ‘formate’ which causes high anion gap acidosis, CNS and ocular injuries.5,6 Formate inhibits cytochrome C oxidase in mitochondria leading to tissue hypoxia and cellular damage disturbing the flow of axoplasm and causing myelinoclastic effect resulting in pathological condition of the eye [6,7].

Intial symptoms of methyl alcohol poisioning are vomiting, headache, confusion, seizures, coma and death.

The symptoms are non specific except for visual disturbances which include blurring of vision, central scotoma and blindness. Ocular examination reveal mydriasis, amaurosis, retinal edema, hyperemia, papilledema and optic atrophy. Laboratory evidence of metabolic acidosis with elevated anion and osmolar gap, decreased bicarbonate blood level with methyl alcohol level > 20 mg/dl confirm the methyl alcohol poisoning as per criteria (Table 1). Imaging study, CT head and MRI brain reveal typical CNS toxicity characteristically bilateral putaminal hemorrhagic necrosis due to selective vulnerability of these regions to methanol toxicity [8]. Rapid decision making, early and aggressive management is crucial to prevent hazardous outcome of methanol toxicity [9].

The first treatment is to secure and maintain airway, breathing and circulation. Initial treatment with sodium bicarbonate 1-2 mg/kg via intravenously bolus is required for patient with pH below 7.3 followed by maintenance infusion till arterial pH is above 7.35. Treatment with ADH inhibitors, fomepizole (4-methyl pyrazole) or ethanol is initiated earlier to delay the metabolism of methyl alcohol to toxic metabolite 'formate' and to prevent its accumulation and toxicity. 5,6,9 Fomepizole is FDA approved. The loading dose is 15 mg/kg intravenously followed by 10 mg/kg every 12 hours, with adjustment for hemodialysis. We couldn't use Fomprizole as it is not available in India. Ethyl alcohol is administered intravenously or orally to maintain the blood level of 100 mg/dl in dosage regimens (Table 2). In our case we use oral ethyl alcohol, but the treatment was a delayed initiation due to late presentation which could not prevent permanent blindness. Treatment with folinic or folic acid 50 mg IV 6 hourly or orally as co-factor therapy accelerates the formic acid elimination. Hemodialysis enhances removal of methanol and formic acid and is indicated in metabolic acidosis, pH <7.3, methonal level >50 mg/dl or visual loss and organ damage [9]. Intravenous methyl prednisolone followed by oral prednisolone or tropical steroids salvage the vision [3,10]. On the spot deaths of two other concurrent victims suggested earliest toxicity of fatal outcome and aided to strong suspicion in the diagnosis of methyl alcohol poisoning.

3. CONCLUSION

The early diagnosis of methyl alcohol poisoning aims at earlier initiation of treatment including ADH inhibitors to prevent formic acid accumulation and hazardous outcome of methanol toxicity – permanent blindness, coma and death. Late Presentation of our case led to typical clicinico-patho-radiological manifestation revealing severe metabolic acidosis with high anion gap, typical ocular and selective neurotoxicity, where the permanent blindness could not be prevented even with aggressive treatment. Rapid recognition, early and aggressive management has been emphasized to prevent the hazardous outcome.

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