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METHANOL POISONING- A REVIEW

Neurology

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ABSTRACT

Methanol toxicity is an uncommon but serious poisoning. Its adverse effects are primarily due to its major metabolite formic acid and lactic acid resulting from cellular hypoxia. Symptoms including abdominal pain and loss of vision can appear a few hours to a few days after exposure. History of exposure, increases in serum osmolality and anion gaps can point to methanol poisoning. Definitive diagnosis requires measurement with gas or liquid chromatography, which are laborious and expensive procedures, not readily available at many centers. Treatment can include administration of ethanol or fomepizole, both inhibitors of the enzyme alcohol dehydrogenase to prevent formation of its metabolites, and hemodialysis to remove methanol and formate. In this review article, the clinical manifestations, the value and limitations of current and new diagnostic and treatment measures are discussed.

KEYWORDS

Methanol, Formic acid, osmolality, hemodialysis.

INTRODUCTION:

Methanol (CH3OH) is a toxic form of alcohol found in various household and industrial agents. Also known as methyl alcohol or wood alcohol, it is a clear, colourless, volatile, and flammable liquid. The term "toxic alcohols" is a collective term that includes methanol, ethylene glycol, and isopropyl alcohol. Methanol poisoning is most often due to accidental or intentional ingestions, and accidental epidemic poisonings due to distilling and fermenting errors and beverage contamination. Products that contain methanol include windshield washer fluid, gas line antifreeze, carburetor cleaner, copy machine fluid, perfumes, food warming fuel and other types of fuels [1, 2]. Methanol toxicity can occur via ingestion, dermal absorption, and inhalation. The most common reported ingestions are secondary to drinking windshield washer fluid as a suicide attempt. Accidental ingestions can occur via exploratory behavior in children [3]. Individuals at risk include toddlers and young children exploring their environment, alcoholics, and suicidal individuals. Most cases are isolated incidents; however, epidemics have also occurred secondary to tainted ethanol and improper distilling.

PATHOPHYSIOLOGY:

Methanol is absorbed rapidly via the upper gastrointestinal tract in less than 10 minutes after ingestion. Methanol is not protein-bound and is absorbed directly into the total body water compartment with a volume of distribution of approximately 0.7 L/kg. Serum concentrations peak immediately after absorption and follow a zero-order elimination rate.

Metabolism occurs mainly in the liver. [Figure1]

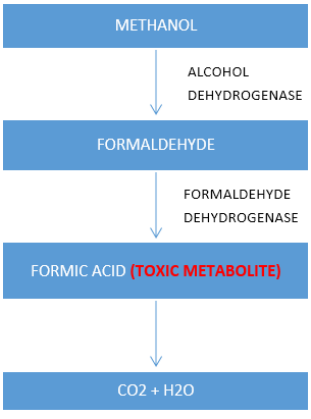

Figure 1. Metabolism Of Methanol

Each of these two oxidation steps is associated with a reduction of NAD to NADH. This enzymatic metabolism provides a zero-order elimination rate of about 8 to 9 mg/dL/h when methanol concentration is between 100 and 200 mg/dL. Formic acid is not easily eliminated and mostly accumulates, while a small amount in its unprotonated form, formate, interacts with folate to create carbon dioxide and water for exhalation. Unmetabolized methanol is not sufficiently cleared through the kidneys or the lungs and has an effective half-life of about 30 to 85 hours [4].

CLINICAL FEATURES:

Patients who present within the first 12 to 24 hours following ingestion may appear normal, and this is described as the latent period. Nausea, vomiting, and abdominal pain subsequently ensue, followed by central nervous system (CNS) depression and hyperventilation as metabolic acidosis occurs. Ocular symptoms associated with retinal toxicity in the form of blurred vision, decreased visual acuity, photophobia, and "halo vision." Physical exam findings may include papilledema, optic disc hyperemia, and pupillary defects on fundoscopic evaluation. Symptoms associated with basal ganglia toxicity are not detectable early on due to mental status depression and the acuity of illness. Without treatment, patients may progress to coma, respiratory or circulatory failure and death.

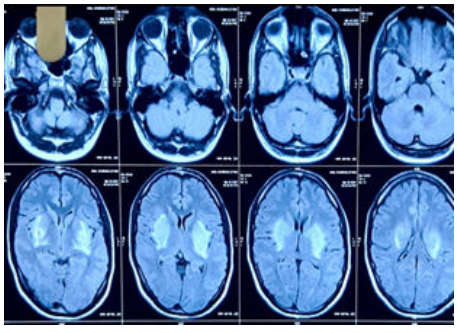

Figure 2. Bilateral Symmetrical Putaminal Hyperintensities.

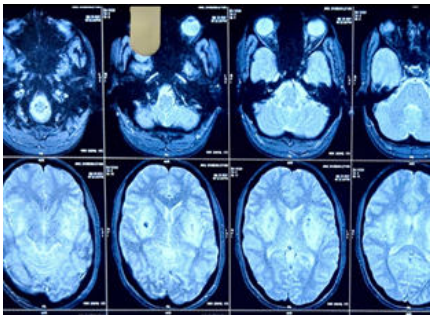

Figure 3. Same Patient Gre Sequence Shows Blooming In Bilateral Putamen Suggestive Of Putaminal Necrosis.

EVALUATION:

An electrocardiogram, basic metabolic panel, and acetaminophen concentration, urinary toxicology panel should be obtained on all toxicology patients with suspected self-harm. Additional tests to be considered when self-harm is a concern are a complete blood count, liver functions, renal functions, lipase, pregnancy status, serum or urine ketones, lactate, ethanol and salicylate concentrations.

Toxic alcohol concentrations are confirmatory and are measured by gas chromatography, which is not readily available in all healthcare facilities. In the case of methanol, a formate concentration may be assessed to correlate with acidosis or any clinical findings of end-organ damage. Many prefer to utilize the measurement of the osmolar gap for further risk stratification in the early presenting patient. An increased osmolar gap is nonspecific and indicates the presence of any osmotically active agent, such as an alcohol. There is an inverse relationship between the osmolar gap and the anion gap [5].

Serum osmolality = [2(Na) + BUN/1.6 + Glucose/18 + Ethanol/4.6]

Toxic alcohol exposure is confirmed when a serum concentration demonstrates the diagnosis. It should be suspected in a patient with developing metabolic acidosis with an elevated anion gap, preceded by an osmolality gap that is decreasing over time, with associated symptoms as described above. Lactate and ketones may be detectable but are nonspecific [6]. MRI brain may show characteristic bilateral putaminal involvement with necrosis. [Figure 2, 3]

Newer advancements include Dipstick impregnated with alcohol oxidase strip which detects methanol, ethanol, and ethylene glycol based on enzyme alcohol oxidase and Liquid-based test of saliva using enzyme or oxidizing agents which uses combination of enzymes (alcohol oxidase or dehydrogenase) and/or oxidizing agents such as potassium permanganate and sodium periodate.

TREATMENT:

Indications of treatment:

An elevated methanol concentration and severe or progressing acidosis, despite resuscitation, with clinical suspicion of methanol ingestion.

When to start the treatment varies with each individual. No doubt, if suspicion of toxicity is suspected without symptoms, 12 hrs of observation may be considered as there may be a latent period before symptoms manifest or some authorities start therapy as soon as possible after the ingestion, even with mere suspicion of toxicity. Considering the zero-order kinetics and the median half life maximum upto 85 hours (3-4 days) therapeutic treatment is controversial and no guidelines are laid down for management after 3-4 days of ingestion of methanol, the decision would depend upon the discretion of the treating physician. Most conservative recommendations are to start treatment if the methanol concentration is greater than 20 to 25 mg/dL. However, if metabolic acidosis is mild or not present, and there is no evidence of end-organ toxicity, then a methanol concentration of 32 mg/dL is an appropriate starting point for treatment as molar calculations indicate this would correlate with a maximum of 10mmol/L of a toxic metabolite (formate). When methanol concentration is not attainable, then an appropriate indication for treatment should be when bicarbonate progresses below 15mmol/L or if there is evidence of retinal toxicity.

Treatment options for methanol toxicity include following measures:

a. Supportive care- intensive care monitoring is needed along with continuous vitals, basic metabolic profile and acid-base, anion gap monitoring. Patient is administered with iv fluids i.e saline or DNS with multivitamin (including thiamine).
b. Fomepizole (Antizole, 4-Methylpyrazole or 4MP)- serves as alcohol dehydrogenase inhibitor to stop the conversion of methanol to its toxic metabolite, formate. When alcohol dehydrogenase is inhibited, clearance of methanol is prolonged from approximately 8.5 mg/dL/hr to an effective half-life of 45 to 90 hours. Fomepizole is given intravenously, with a loading dose of 15 mg/kg, and then maintenance dosing of 10 mg/kg every 12 hours for 4 doses or until the methanol concentration is less than 32 mg/dL with a normal acid-base status. If additional dosing is required beyond 4 maintenance doses, then dosing increases to 15 mg/kg every 12 hours due to autoinduction of increased metabolism. During dialysis, fomepizole should be dosed every 4 hours as it is dialyzable.
c. Ethanol- It also serves as alcohol dehydrogenase inhibitor. Dosing of ethanol is more complicated and difficult to monitor. It may be given orally or intra-venously. However, it should only be given if fomepizole is unavailable. Empirically, 10% intravenous ethanol may be administered with a loading dose of 8 mL/kg over 30 to 60 minutes, followed by maintenance dosing of 1 to 2 mL/kg per hour. Maintenance dosing is doubled during dialysis. Oral dosing may be calculated using the above equation for serum alcohol concentrations by using 100 mg/dL for the serum concentration and then solving for the amount ingested. Empirically, 50% (100 proof) oral ethanol may be administered with a loading dose of 2 mL/kg followed by 0.2 to 0.4mL/kg per hour. Maintenance dosing is doubled during dialysis.
d. Dialysis-

Box 1. Indications for Hemodialysis for Treatment of Methanol Intoxication

American Academy of Clinical Toxicology Practice Guidelines[13]

pH < 7.25 to 7.35
or visual signs and/or symptoms
or decreased vital signs despite intensive supportive care
or kidney failure
or substantial electrolyte disturbances unresponsive to supportive care
or serum methanol concentration > 50 mg/dL

Extracorporeal Treatment in Poisoning Workgroup[6]

pH < 7.15
Severe visual defects
or coma
or worsening vital signs despite intensive supportive care
or kidney failure
or serum methanol:
>70 mg/dL with fomepizole
>60 mg/dL with ethanol
>50 mg/dL in absence of inhibitor

[7, 8]. Patients with a toxic methanol ingestion should be strongly considered for hemodialysis.
e. Folate- There IS theoretical benefit as it may enhance the metabolism of the toxic metabolite, formate, to carbon dioxide and water.
f. Steroids- Intravenous high-dose methyl prednisolone may have benefits in the treatment of methanol optic neuropathy. Several studies reported that it is important to start treatment as soon as possible. Intravenous methylprednisolone given 6 days after methanol ingestion is not effective in improving vision [10].

PROGNOSIS:

Patients often recover when prompt diagnosis and treatment occur. Retinal toxicity and basal ganglia toxicity may result in permanent symptoms. When patients present late or diagnosis is not recognized in a timely fashion, significant morbidity and mortality can occur.

REFERENCES:

1. Chan APL, Chan TYK. Methanol as an Unlisted Ingredient in Supposedly Alcohol-Based Hand Rub Can Pose Serious Health Risk. Int J Environ Res Public Health. 2018 Jul 09;15(7).
2. Ahmed F, Khan NU, Ali N, Feroze A. Methanol poisoning: 27 years experience at a tertiary care hospital. J Pak Med Assoc. 2017 Nov;67(11):1751-1752.
3. Holt NR, Nickson CP. Severe methanol poisoning with neurological sequelae: implications for diagnosis and management. Intern Med J. 2018 Mar;48(3):335-339.
4. Zakharov S, Pelclova D, Diblik P, Urban P, Kuthan P, Nurieva O, Kotikova K, Navratil T, Komarc M, Belacek J, Seidl Z, Vaneckova M, Hubacek JA, Bezdicek O, Klempir J, Yurchenko M, Ruzicka E, Miovsky M, Janikova B, Hovda KE. Long-term visual damage after acute methanol poisonings: Longitudinal cross-sectional study in 50 patients. Clin Toxicol (Phila). 2015 Nov;53(9):884-92.
5. Ashurst JV, Nappe TM. Methanol Toxicity. [Updated 2020 Jun 26]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2021 Jan-.
6. Golden R, Valentini M. Formaldehyde and methylene glycol equivalence: critical assessment of chemical and toxicological aspects. Regul Toxicol Pharmacol. 2014

Jul;69(2):178-86.
7. Barceloux DG, Bond GR, Krenzelok EP, Cooper H, Vale JA. American Academy of Clinical Toxicology practice guidelines on the treatment of methanol poisoning. J Toxicol Clin Toxicol. 2002;40(4):415-446.
8. Roberts DM, Yates C, Megarbane B, et al. Recommendations for the role of extracorporeal treatments in the management of acute methanol poisoning: a systematic review and consensus statement. Crit Care Med. 2015;43(2):461-472.
9. 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. doi: 10.1089/jop.2010.0145. PMID: 21663445.
10. Triningrat AAM, Rahayu NMK, Manuaba IBP. Visual acuity of methanol intoxicated patients before and after hemodialysis, methylprednisolone and prednisone therapy. J Oftalmol Indonesia 2010;7:129-32.