**Abstract**

**Background**: Many outbreaks of methyl alcohol poisoning have been reported from India. Early and aggressive management with bicarbonate, ethanol and hemodialysis in patients having significant toxicity will decrease mortality and improve patient’s outcome. Our experience of retro bulbar steroid injection indicates that it may improve visual outcome.

**Materials and Methods**: Hospital based study of patients admitted to V.S. Hospital during the outbreak of methanol poisoning in Ahmedabad. Patients were identified by history supplemented by ophthalmic examination and biochemistry. A stepwise treatment was undertaken i.e. aggressive treatment with bicarbonate, ethanol and institution of hemodialysis in patients who had refractory high anion gap metabolic acidosis, visual signs and symptoms, deteriorating vital signs and serum methanol level > 50 mg/dL. Patients who were having optic neuritis were given retrobulbar steroids.

**Results**: Total 63 males were admitted between 18 to 60 years. 17 patients were terminally ill with hypotension, could not be subjected for hemodialysis and expired. Of remaining 46 patients, 20 responded to conservative management whereas 26 underwent hemodialysis of which only 3 died.

**Conclusion**: Patients undergoing hemodialysis showed immediate improvement in their clinical and biochemical parameters with rapid reductions of methyl alcohol levels below the toxic range with subsequent reduction in morbidity and mortality. All the patients given retrobulbar corticosteroid injection showed improvement in fundoscopic examination and perimetric charting with maximal improvement in visual acuity in hemodialysed patients.

**Introduction**

Methyl alcohol is a cheap and potent adulterant used in manufacture of illicit liquors. Many outbreaks of methyl alcohol poisoning have been reported from India.\(^1\)\(^2\) The present study describes our experience in the management of patients with methyl alcohol poisoning and emphasizes the role of early and aggressive treatment with bicarbonate, ethanol and of hemodialysis in patients having significant toxicity.\(^3\)

**Materials and Methods**

This study involved 63 patients who were admitted to Vadilal Sarabhai General Hospital during methanol poisoning outbreak in Ahmedabad in 2009. Our present study does not truly represent the burden of this outbreak since only a fraction of the patients were directed to this institution. Patients were selected according to criteria mentioned in Table 1 and managed in a stepwise manner as mentioned in Table 2. Fomepizole, a FDA approved drug was not available, so not used as our treatment modality. The dose of ethanol and criteria for selection of patients who needed dialysis is mentioned in subsequent tables. Complete ophthalmic evaluation was undertaken and all those who had visual toxicity, retrobulbar triamcinolone was injected irrespective of severity of damage.

**Results**

Total 63 male patients between 18 to 60 years were admitted. Most of them had consumed 150 to 250 ml of alcohol 24-48 hours back. All except one had ABGA suggestive of high anion gap metabolic acidosis with hypokalemia. Seventeen patients had hypotension, could not undergo hemodialysis and died. Of remaining 46 patients, 20 responded to conservative management, rest 26 underwent hemodialysis and only 3 died. Patients who underwent hemodialysis showed rapid improvement in their clinical and bio chemical parameters with rapid reduction in methyl alcohol levels below the toxic range with subsequent reduction in morbidity and hospital stay. Ethyl alcohol drip was admitted in patients managed conservatively up to one week unlike hemodialysed patients who were administered intravenous ethyl alcohol for 3 days. Ophthalmic examination revealed dilated pupils with sluggish reaction to light (20%), hyperemia of disc with blurred disc margin (55%), retinal congestion (45%) and varying degree of vision loss (Visual blurring 60%, Below finger counting 10%). All these patients were given retrobulbar corticosteroid. They improved with declined retinal congestion and edema (75%). These patients were followed up and showed improvement in fundoscopic examination and perimetric charting. The recovery was maximal in patients who underwent hemodialysis.

**Discussion**

Methanol, also known as wood alcohol, is a commonly used organic solvent, the ingestion of which has severe potential ramifications. It is a constituent in many commercially available...
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 osmolar gap >10 mOsm/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. Osmolar gap > 10 mOsm/kg

`Any one of the three`

Table 2*: Stepwise algorithm of management

<table>
<thead>
<tr>
<th>Suspected or Confirmed Methanol Poisoning</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
</tr>
<tr>
<td>Supportive care as needed</td>
</tr>
<tr>
<td>Administer folic acid or folic acid (Leucovorin)</td>
</tr>
<tr>
<td>PH &lt; 7.3</td>
</tr>
<tr>
<td>Fomepizole Available?</td>
</tr>
<tr>
<td>Yes</td>
</tr>
<tr>
<td>Administer ethanol per Table 3</td>
</tr>
<tr>
<td>Administer bicarbonate to correct pH to ≥ 7.3</td>
</tr>
<tr>
<td>Administer ethanol per Table 3</td>
</tr>
<tr>
<td>Hemodialyze</td>
</tr>
<tr>
<td>Continue until serum methanol concentration &lt; 20 mg/dL</td>
</tr>
</tbody>
</table>

Although this algorithm may be justified in individual patients based on the clinical judgement of the treating physician.

These guidelines are based on the data presented in this document. Where data was insufficient to validate a specific recommendation the Committee's best judgment, based on the available data is presented. This algorithm should be considered to represent general guidelines. Deviations from this algorithm may be justified in individual patients based on the clinical judgement of the treating physician. & alamed research/scribd

Table 3: 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

<table>
<thead>
<tr>
<th>Hospitalized</th>
<th>Alcoholic</th>
<th>Methanol level</th>
<th>10% ethanol IV (mL/kg/hr)</th>
<th>40% ethanol PO (mL/kg/hr)</th>
<th>95% ethanol PO (mL/kg/hr)</th>
<th>Hemodialysis with 10% ethanol IV (mL/kg/hr)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Moderate</td>
<td>1.4</td>
<td>0.3</td>
<td>0.15</td>
<td>2.7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Drinker</td>
<td>2</td>
<td>0.4</td>
<td>0.2</td>
<td>3.9</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chronic</td>
<td>0.8</td>
<td>0.2</td>
<td>0.1</td>
<td>2.7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Drinker</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nondrinker</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

Industrial solvents and in poorly adulterated alcoholic beverages. Toxicity usually occurs from intentional overdose or accidental ingestion and results in metabolic acidosis, neurologic sequel, and even death. Methanol toxicity remains a common problem in many parts of the developing world, especially among members of lower socioeconomic classes.

Methanol is readily and rapidly absorbed from all routes of exposure (dermal, inhalation and oral), easily crosses all membranes, and thus is uniformly distributed to organs and tissues. The potentially lethal dose of methanol is variable. The lowest reported is 30 mL. The peculiarity of methanol poisoning is the latent period between the ingestion of the alcohol and the appearance of manifestations. The latency may be related to the concomitant ingestion of ethanol which affects the metabolism of methanol. Methanol has relatively low toxicity. Methanol is metabolized in a sequential fashion, principally in the liver by alcohol dehydrogenase leading to formation of formaldehyde. The latter undergoes oxidation to formic acid, facilitated by formaldehyde dehydrogenase. The conversion of formaldehyde to formic acid is very rapid with a half-life of 1-2 minutes. There does not appear to be any accumulation of formaldehyde in the blood. Formate metabolism is dependent upon the presence of tetrahydrofolate to form 10-formyltetrahydrofolate that can be metabolized to carbon dioxide and water or alternative metabolic pathways. The half-life of formate is 20 hours in humans.

Nicholls has demonstrated that formic acid can inhibit cytochrome C oxidase activity in intact mitochondria, in submitochondrial particles, and in isolated cytochrome aa3. Formic acid binds to the sixth coordination position of ferric heme ion in cytochrome oxidase, preventing oxidative metabolism. This is due to the affinity of formic acid for ferric iron moiety. This affinity is also thought to be causing methemoglobinemia seen rarely in cases of severe methanol poisoning. The inhibition of cytochrome oxidase complex at the terminal end of the respiratory chain in the mitochondria leads to “histotoxic hypoxia.” The binding of formic acid to cytochrome oxidase is similar to that seen with other toxins such as cyanide, hydrogen sulfide, and carbon monoxide, although formic acid is a less potent inhibitor. The inhibition of cytochrome oxidase by formic acid increases with decreasing pH. This suggests that the active inhibitor is the undissociated acid as the concentration of the latter increases with fall in pH and as the inner membrane of the mitochondria is only permeable to the undissociated acid.

Therefore, as the pH falls, cytochrome oxidase inhibition is potentiated and the onset of cellular injury is hastened.
The symptoms of methanol poisoning are non-specific except for the visual disturbances. Ocular changes consisting of retinal edema, blurring of the disc margins, hyperemia of the discs and optic atrophy are late sequel and are characteristic of poisoning.\(^8_{,11}\) The terminal event is often respiratory arrest. The fatal period is from 6-36 hours. Metabolic acidosis is the most dramatic and is probably due to the accumulation of formic acid.\(^9_{,10}\) The ocular changes correlate to the degree of acidosis.\(^8_{,10}\) The ocular changes correlate to the degree of acidosis.\(^8_{,10}_{,11}\) Retinal damage is believed to be due to the inhibition of retinal hexokinase by formaldehyde, an intermediate metabolite of methanol.\(^10\)

Ethyl alcohol used, delays metabolism of methyl alcohol to its toxic metabolites by competing for alcohol dehydrogenase.\(^14\) Maintenance of serum ethanol level above 100 mg% is required.\(^15\) Folinic acid also increases metabolism of formates and prevents complications.\(^16\) Fomepizole(4-methyl pyrazole) is a direct alcohol dehydrogenase antagonist\(^17\) which is FDA approved for treatment but not available in India.

Hemodialysis whenever available should be used as a treatment modality in classified patients such as those having persistent refractory high anion gap metabolic acidosis, visual and mental obtundation, >30 ml of methyl alcohol ingestion or >50mg/dl of blood levels,\(^18,19\) deteriorating vital signs despite intensive supportive care, renal failure or significant electrolyte disturbances unresponsive to conventional therapy.\(^20\)

Intravenous or topical steroid therapy could salvage vision in patients having retinal toxicity.\(^21\) Our experience of retrobulbar injection of triamcinolone\(^4\) indicates that it may improve visual outcome. Steroids are helpful in alleviating signs of retinal inflammation. But as the retinal toxicity is due to accumulation of toxic metabolites of methanol, treatment with Folinic acid and Hemodialysis cause removal of these products and in our study significant visual improvement is noted in patients who underwent hemodialysis.\(^14\)

**Acknowledgement**

We would like to express our respect and gratitude to our Alma-mater ‘Sheth K.M. School of Postgraduate and Research’ for the foundation they laid in shaping our careers.

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**References**


