ABSTRACT

Mass intoxication due to methanol is often heard from all parts of the world. Methanol is a highly toxic substance that is associated with over 25% fatality rate, irrespective of the treatment. The present article reviews clinical and pathological findings observed during clinical forensic examinations of twelve victims and five fatalities due to mass methanol intoxications. Blurred vision was observed in 11 patients including five cases with permanent loss of vision. Eight patients showed hypoxic changes. Nausea and vomiting were observed in seven cases. Urine samples obtained from all our victims during 12 - 24 hours of the incident showed traces of Methanol, Formic acid and Formaldehyde.

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The presence of above substances in association with characteristic clinico-pathological findings including permanent visual defects are confirmatory of methanol intoxication. However, authors were unable to correlate plasma formic acid and formaldehyde levels to pathological findings as no blood samples were obtained during early stages of management in medical wards.

Keywords: Methanol intoxication; loss of vision, ethanol.

1. INTRODUCTION

Abuse of illegally produced alcohols, that results in significant morbidity and mortality, is frequently heard from most regions of the Africa, Asia [1] and America. The Sri Lankan alcohol industry as well as the consumption of all forms of alcohol including illicitly distilled varieties, has reached a new height since the conclusion of the North East war [2]. In fact the liquor producing is one of the most profitable industries and the volume of liquor produced maintained an increasing global trend. Alcohol abuse being recognized as one of the main risk factors for increasing prevalence of non-communicable diseases in Sri Lanka [3]. Recent local series showed reckoning number of Methanol intoxications and self poisoning [4] cases, especially from rural communities in Sri Lanka [5], though the manufacture of alcohol has been strictly regulated in accordance with the conditions stipulated in the Government Gazette Notification of No. 1232\12 of 18 of April 2002. According to post-mortem registry of the Karapitiya Teaching Hospital, there had been several incidents of accidental methanol poisoning in Galle area in year 2005. The most commonly used illicit alcohol, that contains 35 to 40% ethanol, is known as “Kasippu” which is usually distilled out of sugar syrup and other locally available fruits. It contains a variety of fusel alcohols including methanol due to uncontrolled production techniques.

Methanol may be disseminated through indoor air, water, food, outdoor air or agricultural products and sprays [6]. Methanol can be absorbed into the body by inhalation, ingestion, skin contact, or eye contact. Ingestion is an important route of exposure. Ingestion of methanol may result in acute brain lesions with permanent neurological manifestations that may be life-threatening at times. The present article reviews clinical and pathological findings observed during twelve clinical forensic examinations and five autopsies due to mass methanol intoxications [17 cases].

2. METHODOLOGY

The study has been conducted at the Forensic Medicine Unit of the Karapitiya Teaching Hospital in Galle, Southern Sri Lanka. The Clinico-pathological findings of medico-legal examinations of 17 cases [12 clinical cases and 5 autopsies] due to methyl alcohol intoxications, [Hypoxia, Nausea, Vomiting, Headache, visual impairment], laboratory investigations [Hb, PH, PCO2, Na+, K+, Blood urea, Blood ethanol, Urine ethanol, Formaldehyde and Formic acid], Bed Head ticket records and autopsy features were recorded. All details were entered into database using MS Access 2000 worksheet and summarized to tabulated format. Then findings of each case were qualitatively analyzed and compared with the data available in the literature.
Table 1. Clinical examination findings and autopsy details of 17 cases

<table>
<thead>
<tr>
<th>Case no</th>
<th>Amount of blood given</th>
<th>Use of ethanol</th>
<th>Clinical sign and symptoms- Blurred vision</th>
<th>Laboratory investigation</th>
<th>Government analysis report</th>
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</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Anoxia</td>
<td>Nausea</td>
<td>Vomiting</td>
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<td>01</td>
<td>1 pack</td>
<td>1 dram</td>
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<td>02</td>
<td>2 pack</td>
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<td>-</td>
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<tr>
<td>03</td>
<td>2 pack</td>
<td>1/2 bottle</td>
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<tr>
<td>04</td>
<td>2 pack</td>
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<td>+</td>
<td>+</td>
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<td>05</td>
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<td>12</td>
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</tr>
<tr>
<td>13 to 17</td>
<td>Showed minimal symptoms and discharged after initial treatment/ No investigations were done</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>
3. RESULTS OF CLINICAL EXAMINATION AND AUTOPSY FINDINGS:

The cases 1 to 5 died within 48 hours of admission. Cases 13 to 17 showed minimal symptoms, treated and discharged. Cases 1 to 12 showed traces of methyl alcohol, formaldehyde and formic acid in the urine [ante-mortem] samples. Ethanol concentration of blood samples varies from 4 to 246 mg %. Patients No 6 and 8 developed respiratory distress and ventilated in intensive care unit. Patient No 12 has exclusively high [249 mg%] blood alcohol and did not show significant clinical signs of methyl intoxication. The Blurred vision was observed in 11 patients and five out of them [cases 6 -10] have suffered a permanent loss of vision. Eight patients showed hypoxic changes. Nausea and vomiting were observed in seven cases. Two deceased and two survivals showed high blood and urine ethanol levels over 100mg%. Traces of methanol, formic acid and acetaldehyde were present in urine samples of all victims. Findings are summarized in Table 1.

Autopsies showed cerebral oedema, hypoxic and necrotic changes of white matter in all five cases, with necrosis of basal ganglia in two cases. No cerebral haemorrhages were observed. Acute tubular necrosis and moderate fatty changes of hepatocytes were seen in all deceased persons. Lung tissues showed congestion and interstitial oedema. The cause of deaths was attributed to multiorgan [cerebro-hepato-renal] failure due to methanol toxicity due to establishment of anion gap.

The significantly high levels of ethanol found in victims 5, 6 and 12 were attributed to ingestion of ethanol as a part of therapeutic measures. Headache, abdominal cramps and blurred vision were most constantly observed clinical features in over 80% victims. There was no significant difference of blood urea, Na⁺, K⁺ levels between survivals and deceased persons.

4. DISCUSSION

Methanol is the lightest form of alcohol, known as wood alcohol, which is closely related to ethanol, but is much more toxic, even lethal and usually present in small quantities in many alcoholic beverages, especially those home brewed varieties. Methanol poisoning occurs in isolated as well as epidemic circumstances. A recent Cuban news report showed mass fatality where seven people have died of poisoning after consuming black-market methyl alcohol and 41 others remained hospitalized [7]. Methanol intoxication is heard from all parts of the world [8]. The majority victims of mass scale ethanol poisoning belong to lower socio-economic layers. The recent announcement of the Health Ministry of Kenya stated that samples of alcoholic beverage responsible for the death of over 80 people in Kenya had been found to contain 70 – 100% methanol [9]. The victims of the present incident are also from low-income casual labour community off Galle region in Southern Sri Lanka, who habitually consume low cost alcoholic beverages that are illegally produced in local villages. The availability, community drinking pattern and low cost due to hiding from taxation make them very attractive for low-income groups.

4.1 Brief History

The present article is pertaining to medico-legal investigation of alcoholic cohabitants who had taken illicit alcohol called “Wine” which is made out of wine spirit were fallen ill with the signs of vomiting, severe headache, disturbances of vision and deteriorated
consciousness and admitted to the Karapitiya hospital. Five persons had relatively mild symptoms and discharged after initial symptomatic treatment. Seventeen victims are hospitalized, five out of them died within 48 hours of admission while four others suffered a permanent loss of vision.

Illicit alcohol manufacturers in Sri Lanka used to ferment beverages from freely available sugar bases, fruits, remnant of sugar cane mould, neera or unfermented sap from coconut etc. These illicit liquors, called Kasippu [10] are widely available throughout the country and enjoy higher demand due to low cost. These homemade beverages usually contain small amounts of methanol, insufficient to cause significant clinical symptoms. In fact, this particular seller has used commercially available so-called ‘wine spirit’ that meant for preheating and igniting of kerosene oil based ‘Petromax’ mantle lamps [11]. It contained mixture of ethyl alcohol, methyl alcohol and several other accelerants. The sellers are well aware of toxicity of the ‘wine spirit’ and apply surface burning technique to burn-out highly volatile methyl alcohol and other fusel alcohols. The procedure is entirely experience based which fails to achieve 100% purification at all times. The present mass intoxication was due to remnants of methyl alcohol in ‘wine spirit’ following incomplete detoxification procedures.

Methanol is a colorless liquid with a mild alcohol odor which is widely used as a chemical feedstock to produce a variety of consumer products. Methanol is toxic to humans, and is readily absorbed by ingestion and inhalation, and more slowly by skin exposure. Methanol is produced naturally in the anaerobic metabolism of many varieties of bacteria, and is commonly present in small amounts in the environment.

However, methanol is naturally present within the human body in small quantities from eating fruits and vegetables. According to the FDA, as much as 500 milligrams per day of methanol is safe in an adult’s diet [12]. Methanol is rapidly absorbed and distributed in all body tissues, undergoes extensive metabolism but is relatively slow (t½ is about 24 h) and is primarily as formic acid in the urine. Urine samples obtained from all our victims during 12 -24 hours of the incident showed traces of Methanol, Formic acid and Formaldehyde.

The enzyme alcohol dehydrogenase is responsible for metabolism of methanol (Fig. 1). Ethanol has a higher affinity for this enzyme and is preferentially metabolized [13]. Methanol is converted to formaldehyde and formic acid in the liver. Further metabolism of formic acid to carbon dioxide is dependent on folate [14].

![Metabolic pathways of ethanol and methanol](image)

**Fig. 1. Metabolic pathways of ethanol and methanol**
Serum methanol levels of greater than 20 mg/dL necessarily leads anion gap metabolic acidosis due to unmeasured acids (Fig. 2) and subsequent development of ocular injury. Formic acid is highly ocular toxic which causes permanent damage to the retina and optic nerve. Metabolic acidosis associated with an increased anion gap includes lactic acidosis, ketoacidosis, the acidosis associated with renal failure, and several types of poisoning including salicylate, methanol, ethylene glycol, toluene and paraldehyde [15]. The victims of our series showed significant disturbances of Na+ and K+ Ion levels with increased blood urea levels.

Visual changes with methanol poisoning are due to microtubule and mitochondrial destruction in the retro-laminar optic nerve [16]. Visual impairments are one of the commonest effects of methanol intoxication, and 70% cases of the present study showed some degree of visual disturbances. The condition often presents as a painless, progressive, bilateral, symmetrical visual decline with variable optic nerve head pallor [17]. Histopathological studies showed circumscribed myelin damage behind lamina cribrosa while axons are intact. The rodent study revealed histopathological changes mostly pronounced in the outer retina with evidence of the inner segment swelling, photoreceptor mitochondrial disruption, and the appearance of fragmented photoreceptor nuclei in the outer nuclear layer [18]. The changes are mostly non-reversible.

The autopsy findings of the present series showed significant changes in the brain tissues. The hypoxic changes and necrosis of the white matter are non-specific to methyl alcohol toxicity [19], whereas necrotic lesions of basal ganglia were highly indicative of methanol toxicity [20]. The changes of the renal tubules and the liver tissues are due to general effects of toxic compounds.

Radiological investigations are essential in the diagnosis of cerebral lesions. CT and MR imaging showed bilateral putaminal hemorrhagic necrosis and subcortical white matter lesions with peripheral contrast enhancement [21]. The permanent loss of vision is attributed to necrosis of brain substances. A range of neuropathological lesions including bilateral hemorrhagic necrosis in the putamen and caudate nuclei, diffuse subcortical white and grey matter necrosis, cerebellar and optic nerve necrosis, and diffuse cerebral edema [22] were noted in MR imaging on victims of methanol intoxication. Unfortunately, no radiological investigations were done during clinical management of victims of the present study.
The exact lethal dose of methanol is not known but most authors believe that the ingestion of 100 ml is critical though fatal outcomes were recorded even with ingestion of 15 ml of 40% methanol solution [23]. The overall clinical picture and autopsy features of our series are characteristic of methanol toxicity, but we were unable to correlate above findings with blood levels of methanol as clinical samples were obtained only after intensive therapeutic measures within 12-24 hours of admission.

In spite of the treatment, morbidity and mortality rate is very high in methanol poisoning. The mortality rate of the present incident is about 27%. Treatment consists of the buffer regulators such as sodium bicarbonate to correct metabolic acidosis and antidote to inhibit the metabolism of methanol to its toxic metabolite, formic acid [24]. The inhibition of alcohol dehydrogenase is fundamental to the treatment of methanol poisoning. A fomepizole, an inhibitor of alcohol dehydrogenase, appears to be safe and effective in the treatment of methanol poisoning [25].

Hemodialysis is one of the effective methods of treatment for methanol poisoning [26]. The victims 1 to 11 of this study had received fresh blood transfusions though its effectiveness is a matter of controversy. Intravenous erythropoietin is said to be effective in the management of methanol induced optic neuropathy [27].

The follow-up studies showed that effects of methanol intoxication persist for long years, and even some patients may develop new neurological complications. The most frequent sequelae found at discharge are visual disturbances and neurological impairment of some kind [28]. However, cases of spontaneous recovery from the methanol related neuropathy has also been reported [29].

5. CONCLUSION

The study further confirms that fatality rate due to methanol intoxication is high [0ver 25%], in spite of the treatment. The presence of formic acid and acetaldehyde in urine samples of all victims shows that their formation is mainly responsible for the toxic effects, specifically for the visual impairments. Clinicopathological findings of our series are in keeping with that of other surveys.

Use of illicit alcoholic beverages is yet a reckoning social and medical issue especially in remote areas of the country. The survivals of our study were appropriately educated about hazards related to consumption of illicit liquor and referred to eye and neurological clinics of the hospital for long term management. The police was provided with detailed medico-legal reports highlighting an importance of preventive measures.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES


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