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CASE REPORT

Eight fatalities due to drinking methanol-tainted alcohol in Pakistan: A case report

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KEYWORDS

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Abstract Methanol has a widespread commercial use as a solvent in paints, varnishes, anti-freeze solutions and denaturant for ethanol. Exposure may occur due to accidental, suicidal ingestion or as a result of consuming adulterated liquor. Fatalities were reported in Pakistan in an incident after consuming methanol-tainted liquor. Postmortem specimens of eight deceased males, ages ranged from 16 to 40 yrs, were submitted for toxicological analysis. Presence of blurred vision, severe metabolic acidosis with decreased serum bicarbonate level, increased serum osmolality and mean anion gap before death strongly suggested methanol toxicity. Headspace gas chromatograph coupled to flame ionization detector was used to quantify volatiles in blood and stomach contents of victims. Lethal levels of methanol in addition to ethanol were detected. The most probable mechanism of methanol-related deaths was sudden cessation of respiration due to inhibition of cytochrome oxidase that led to histotoxic hypoxia.

1. Introduction

Methanol is a common component of paints, varnishes, solvents, anti-freeze solutions and is utilized both in denaturing ethanol and as an alternative fuel source.[1] Pure methanol is colorless and has a faint, slightly alcoholic odor with molecular weight of 32 g/mol.[2] It is easily absorbed through the skin, respiratory tract or gastrointestinal tract causing toxicity. Normal blood concentration derived from endogenous production and dietary source is 0.00015 g/dL or less.[3,4] Dietary sources include fresh fruits/juices, vegetables and dietary products containing aspartame. Minimum lethal concentration in blood is 0.04 g/dL and the smallest amount of methanol reported to cause death is 15 mL of 40% methanol.[5] Methanol is formed in very small amounts during fermentation, the process by which ethanol is made from plant products like grape juice or cereal grains but can cause hang over even in these small amounts. The potential for its presence in drinks made from home-distilled spirits is a serious health risk. Home distillation to make spirits like gin or rum concentrates the levels of both ethanol and methanol and is not technically advanced to separate methanol from ethanol. The methanol content of 20 commercial wines was found to range from 50 to 325 mg/L[6] and of 24 distilled liquors from 13 to 106 mg/L.[7] Methanol poisoning most commonly occur due to accidental, suicidal

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ingestion or as a result of consuming adulterated liquor in sporadic or epidemic circumstances.[1,8]

The consumption and sale of alcohol, irrespective of age, is illegal in Pakistan but still dozens of people lose their lives every year after consuming home-made liquor tainted with methanol. In this article an incident that occurred in July 2013 in Faisalabad, a city in Pakistan's eastern province of Punjab was presented, which resulted in fatalities after ingesting locally distilled methanol-tainted moonshine. An investigation was launched to probe the incident and an inquiry committee was also constituted under the Punjab Home Department to look into the matter. The alleged supplier of the toxic liquor told the police that he had mixed a chemical (methanol) into liquor to make it taste better; he further confessed that he had bought methanol from a homeopathic doctor. A case was then registered by the police registered against brewers and suppliers.

2. Incident report

Eight patients age ranging between 16 and 40 yrs were admitted to the emergency departments of local hospital in Faisalabad, Pakistan after consuming toxic liquor. All the victims were resident of Faisalabad and belonged to labor community. In an attempt to hide the incident from the police, the victim's relatives first took them to private hospitals but when their conditions deteriorated, they were shifted to government hospitals. At the time of admission, they all complained to vertigo, dizziness, nausea, vomiting and visual disturbances. Available clinical laboratory findings of these patients on hospitalization are shown in Table 1.

Victims were kept in the intensive care units but they could not survive. The victims died within 2–3 h of admission in the government hospital. Autopsies were conducted and postmortem specimens of fatalities[9] were submitted to forensic toxicology department of Punjab Forensic Science Agency Lahore for analysis.

3. Materials and method

3.1. Materials

Commercial grade methanol, ethanol, isopropanol, acetone and n-propanol were purchased from Sigma-Aldrich, USA. Hydrochloric acid was purchased from Fisher Scientific (Fair Lawn, NJ, USA). Synthetic drug free blood was obtained from Immunalysis Corporation, USA.

Table 1 Clinical laboratory findings of the eight patients on admission.

Clinical parameters	Normal lab. ranges	Ranges obtained in patients
Serum potassium level (mEq/L)	3.5–5	2.1–6.3
White blood cell count (WBC/μL)	4500–10,000	7600–14,200
Mean corpuscular volume (fl/dL)	80–100	80–104
Mean arterial bicarbonate level (mmol/L)	22–30	5–19
Mean arterial pH value	7.35–7.45	6.95–7.39
Serum amylase level (mg%)	30–110	30–384
Mean serum osmolality (mOsm per kg of water)	270–290	325
Mean anion gap (mEq/L)	12–16	25

3.2. Method

An Agilent 7890A gas chromatograph coupled to flame ionization detector with split injector and Agilent G1888 headspace auto-sampler was used for the analysis of volatiles in postmortem blood and gastric content specimens. The loop, oven and transfer line temperatures of headspace auto-sampler were set to 80, 70 and 90 °C respectively. Injection time was set to 0.5 min whereas oven stabilization time was 1 min with loop equilibration time of 5 sec. Loop fill time and vial pressurization time were set to 0.2 min with vial equilibration time of 7 min. The separation in gas chromatograph was accomplished on an HP-Innowax (PEG) capillary column (30 m length, 320 μm internal diameter, 0.5 μm film thickness). Injections were made in the split mode with the split ratio of 1:1. The injector was held at 200 °C at a pressure of 4.7543 psi. An Agilent split liner without glass wool was used. Septum purge flow was 3 mL/min and split flow was 0.09479 mL/min. Nitrogen carrier gas (99.999% pure, Noor Chemicals Private Limited, Pakistan) flow to the column was set to 1.4 mL/min. The gas saver mode was turned off in order to allow more nitrogen to run through the liner to displace any residual vapors, hence reducing the carry-over. The initial GC oven temperature was 40 °C which was then ramped at a rate of 16 °C/min to 120 °C and held for 0.3 min. Maximum oven temperature was set to 265 °C with equilibration time of 0.5 min. The FID heater temperature was set to 300 °C. The hydrogen gas (fuel gas in FID produced from HydroGen PH200 H_2 generator by Peak Scientific, Scotland UK) and air flow rates were set to 30 and 400 mL/min respectively with a make-up flow of 25 mL/min. The run time was 5.3 min and the retention time of methanol was 3.4 ± 0.1 min. The method was validated according to criteria established by the SWGTOX guidelines for linearity, limits of detection and quantitation, precision and accuracy.[10] The calibrated concentrations (10, 50, 100, 200 and 500 mg/dL) were chosen to encompass the toxic and fatal methanol and ethanol concentrations.

4. Results

Limits of detection and quantitation for both methanol and ethanol were set at 5 and 10 mg/dL, respectively. Method has shown good linearity up to 1000 mg/dL ($r^2 = 0.998$). Intra-assay (5 calibrator concentrations, 5 replicates) and interassay (5 calibrator concentrations on 5 different days) precision was evaluated and determined to be within acceptable parameters (coefficient of variation was 1.8–6.3%). Accuracy was assessed with four different concentrations (analytical variability ranged from −3 to +8 mg/dL of the target).

Postmortem blood and stomach contents specimens of eight deceased males were analyzed as shown in Table 1, toxicological analysis of postmortem blood and stomach contents revealed the following methanol concentrations was 0.04–0.25 g/dL in blood and 0.014–0.06 g/dL in stomach contents; whereas, ethanol concentration was 0.018–0.072 g/dL in blood and 0.025–0.099 g/dL in stomach contents as shown in Table 2. In addition to methanol, ethanol was also detected in blood

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Table 2 Toxicological analysis of postmortem blood and stomach contents in the eight victims.

Analyte detected	Specimen used	Lethal levels (g/dL)	Levels obtained in g/dL
Methanol	Blood	0.04	0.04–0.25
	Stomach contents	0.0073	0.014–0.06
Ethanol	Blood	0.032–1.8	0.018–0.072
	Stomach contents	Not available	0.025–0.099

and stomach contents. Gas chromatographs showing methanol and ethanol in blood and stomach content specimens are shown in Figs. 1 and 2 respectively.

5. Discussion

Methanol is a clear, colorless liquid that has a widespread commercial use. It is used to fortify illicit spirits by bootleggers because it is cheaper than ethanol. When ethanol is not available, the prisoners and others may substitute methanol-containing products for alcoholic beverages. Acute ingestion of as little as 10 mL of methanol can cause permanent blindness and 100–200 mL is fatal. Methanol is rapidly absorbed from the gastrointestinal tract following oral administration with a mean absorption half-life of 5 min.[11] Depending upon the presence or absence of food, peak absorption occurs within 30–60 min.[12,13] After ingestion, methanol may persist in the body for as long as a week. It is water-miscible and distributes in total body water, therefore higher levels are attained in the aqueous and vitreous humors of the eye, CSF and gastric secretions than in blood.[14] Its volume of distribution is approximately 0.60–0.77 L/kg.[11]

Earliest signs of methanol poisoning are difficult to differentiate from the normal effects of ethyl alcohol. Mild symptoms such as nausea, vomiting and abdominal pain develop within an hour and simulate ethanol intoxication. The more significant symptoms, such as headache, dizziness, vertigo and blurred vision, develop after 12–24 hrs. The worst thing is that it takes 12–24 hrs to differentiate methanol intoxication from that of ethanol and people often have had been solidly drunk and sleeping.

Methanol is metabolized to formaldehyde in the liver by alcohol dehydrogenase enzyme. This reaction is slower than the transformation of formaldehyde to formic acid which causes metabolic acidosis.[14] Symptoms of methanol poisoning are non-specific, except for the visual disturbances and the latent period (1–72 hrs) becomes longer if ethanol is co-ingested, or shorter if the amount of methanol is large. Ethanol competes with methanol for alcohol dehydrogenase in the liver, thereby preventing the accumulation of toxic metabolites of methanol in the body. The enzyme has a greater affinity for ethanol than methanol. Therefore, in the presence of ethanol,

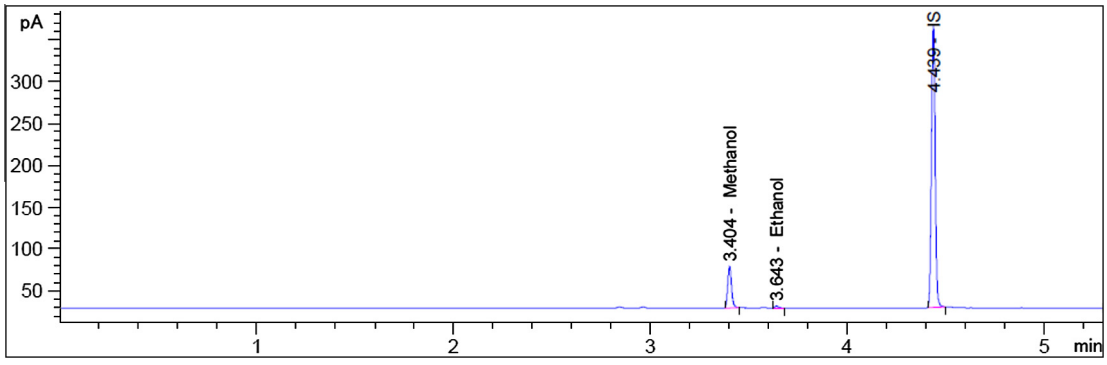

Figure 1 Gas chromatogram showing the peaks of methanol, ethanol and internal standard (n-propanol) in blood specimen of a deceased.

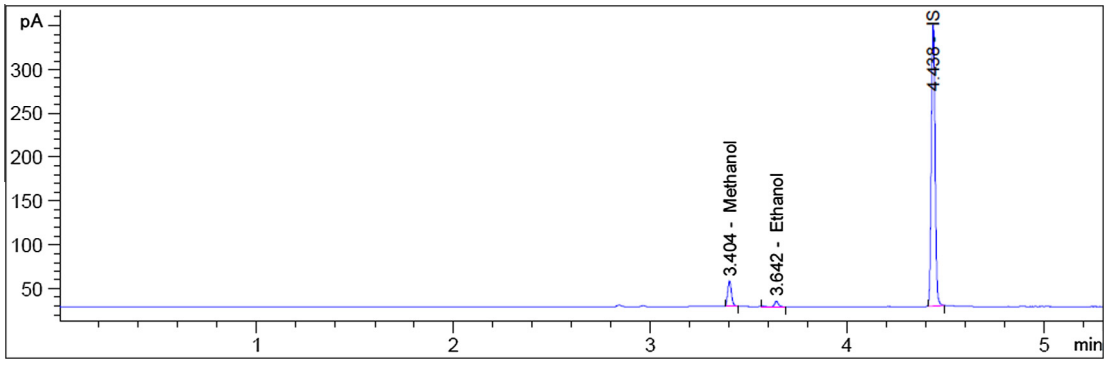

Figure 2 Gas chromatogram showing the peaks of methanol, ethanol and internal standard (n-propanol) in stomach contents specimen of a deceased.

the metabolism of methanol is greatly slowed. Ethanol concentration in the range of 100–200 mg/dL is optimal for saturating alcohol dehydrogenase preventing methanol metabolism leading to inhibition of toxic metabolite formation.[15,16] Methanol exhibits zero-order elimination kinetics with a half-life of 2–24 hrs.[14]

Methanol-related deaths reported in this article were of eight healthy males with a history of alcohol consumption. The presence of blurred vision, severe metabolic acidosis with decreased serum bicarbonate level, increased mean serum osmolality and increased mean anion gap strongly suggested the diagnosis of methanol poisoning. Lethal levels of methanol (0.04–0.25 g/dL in blood and 0.014–0.06 g/dL in stomach contents) were found in addition to ethanol in all victims. Co-ingested ethanol delayed methanol metabolism and resulted in longer latent period (12–72 hrs). The most probable mechanism of methanol-related deaths is sudden respiratory cessation due to histotoxic hypoxia caused by cytochrome oxidase complex inhibition.

Almost all cases of acute methanol toxicity result from ingestion rather than of inhalation or dermal exposure as reported in literature. Methanol poisoning outbreak occurred in Ahmedabad, India in 2009. A total 63 males were admitted to local hospitals, 20 of whom were either terminally ill with hypotension or subjected to hemodialysis were expired. Of the remaining 43 patients, 20 responded to conservative management whereas 23 underwent hemodialysis and survived.[17] Two males (34 and 39 yrs) were admitted in an unconscious state. Both presented with coma and severe acidosis. Toxicological analysis revealed toxic methanol serum levels of 0.54–0.74 g/dL. Despite intensive care and specific therapy, the patients did not survive.[18] In Estonia, 154 patients were admitted with methanol poisoning, 68 (44%) died.[19] In a large methanol outbreak in Norway in 2002–2004, 51 patients were hospitalized with median serum methanol concentration was 0.080 g/dL; 24% were comatose, of whom 67% died.[20] A 26-year old sailor was admitted to the emergency department in a local hospital with hypothermia and in a comatose state. The patient was found unconscious in his cabin by the ship's captain and one of his colleagues confessed they had been celebrating together about 8–12 hrs ago, with alcohol they bought illegally in a harbor store the day before. Laboratory results showed a severe metabolic acidosis and pH of 6.69. On the third day of admission, the ethanol infusion and hemodialysis were discontinued; brain death was officially diagnosed.[21] In two incidents of methanol poisoning in Northern Europe, the mortality rates were 18% and 44%, respectively.[22–24] The American Association of Poison Control Center's Toxic Exposure Surveillance System includes 2418 reports of methanol exposure from 2000.[25] Mass epidemics associated with these circumstances are reported from around the world.[26–31]

6. Conclusion

There are around 150 homeopathic medicine manufacturers in Pakistan who have licenses to manufacture liquor for medicinal purposes but only 10 permit holders are actually operating homeopathic laboratories to manufacture medicines. The rest are involved in the illegal business of selling liquor to bootleggers who sell it to other clients. Some bootleggers mix toxic chemicals which make liquor poisonous. Locally-made bootleg liquor is sometimes added to or substituted for commercially-distilled spirits in drinks because commercial spirits are expensive. According to the Excise and Taxation Department of Pakistan, only qualified homeopathic doctors and manufacturers can get permit of alcohol based on the capacity to use in medicines under policy. They are not allowed to sell alcohol for drinking purposes as it is a crime according to the rules. Methanol-related deaths are almost always the result of greed. The running truism is "methanol poisoning is a result of deliberate addition/adulteration with industrial methanol".

7. Recommendations

1. Awareness needs to be created about the dangers of methanol poisoning.
2. A strong mechanism needs to be formulated to check the sale and manufacturing of alcohol as well as import of methanol in the country.

Funding

None.

Conflict of interest

None declared.

Ethical approval

Necessary ethical approval was obtained from the institute ethics committee.

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