case report

Pitfalls of the Alcohol Dehydrogenase Procedure for the Emergency Assay of Alcohol: A Case Study of Isopropanol Overdose

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We describe a case of ethanol and isopropanol ingestion that resulted in coma. The concentration of ethanol and isopropanol was 0.90 and 1.65 g/liter in serum and 3.12 and 5.34 g/liter in gastric contents. With an enzymatic (alcohol dehydrogenase) method for ethanol determination we obtained erroneous analytical results. Because of partial cross reactivity with isopropanol, ethanol concentration was overestimated and total alcohol (i.e., the contribution of isopropanol) was underestimated. This was recognized by measuring serum osmolality. Differences between measured and calculated serum osmolality that are not accounted for by the serum ethanol concentration as determined by an enzymatic ethanol method must be further investigated by specific methods to see if other alcohols are present.

Additional Keyphrases: drug assay • analytical error • multiple-alcohol ingestion • toxicology

The importance of rapid and precise screening for alcohol in serum from emergency-room patients has been emphasized (1). Serum osmolality measurements, gas chromatography, and an enzymatic method for ethanol quantitation by use of alcohol dehydrogenase (AD; EC 1.1.1.1) were evaluated for use with emergency-room specimens (1). In that study it was shown that use of the enzymatic method for screening could lead to erroneous results because the method is not specific for ethanol, cross reactivity being as great as 40% for isopropanol and 80% for n-propanol. Methanol and acetone do not cross react significantly. Thus erroneous conclusions can be drawn about what the patient has ingested and his clinical condition because total alcohol would be underestimated and ethanol overestimated if only an enzymatic measurement were made. We describe here a case of combined ethanol and isopropanol ingestion. With our proposed screen, multiple alcohol ingestion was indicated but the interference by isopropanol in the enzymatic method was quickly identified by using gas chromatography. This is important in the case of a comatose patient when other causes of coma must be quickly excluded.

Case History

A 45-year-old white male, a self-employed painter, was comatose when brought to the Birmingham Veterans Administration Hospital Admissions Office by family members. His wife stated that she took her husband to work that morning in good health. She received a call from the client at 1130 hours stating that her husband had fallen from a stepladder just a few minutes before and was lying unconscious on the floor.

When seen at the emergency room no seizure activity was noted in this patient. His breath had a sweetish odor. There was no evidence of skull trauma. The following physical and laboratory data were obtained: Blood pressure was 80/60 mmHg, pulse 90/min, and respiration 14/min and shallow. Dipstick tests for urinary glucose and ketones were negative. Data on arterial blood gases with the patient breathing room air were: pH 7.25, $pO_2$ 70 mmHg, $PCO_2$ 60 mmHg. Values for electrolytes were: sodium 145, potassium 4.4, and chloride 105 mmol/liter; bicarbonate 30 mmol/liter; blood glucose 1.61 g/liter; serum urea nitrogen 90 mg/liter; and creatinine 12 mg/liter. Serum osmolality was 369 mOsm/kg of water with a serum ethanol concentration of 1.86 g/liter by an enzymatic alcohol dehydrogenase (AD) method run on the Du Pont aca. A trace (+) of ketones was present in the serum.

The patient was intubated and placed on a respirator for respiratory support because of breathing difficulties.

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Received June 30, 1977; accepted Nov. 8, 1977.
Stomach lavage showed no evidence of pills. Thin-layer chromatography of gastric washings gave negative results for addictive and basic drugs. The serum was negative for salicylates. Phenobarbital determined by enzyme immunoassay was negative. No urine was available for drug screening.

The family stated that the patient had been known to drink ethanol heavily in the past, but had had no more than a few beers during the past week. The patient was said to have ingested after-shave lotion in the past, but no medicines or toilet substances were missing in his home or the home where he was working on that morning. There was no history of suicide attempts or drug abuse.

Method of Further Study, and Results

The osmolality, calculated by the formula previously described (1, 2),

\[ \text{mOsm/kg of water} = \frac{1.86 \text{[Na}^+\text{]} + (\text{glucose/18}) + (\text{serum urea N/2.8})}{0.93} \]

gave a value of 304. The difference between the measured and calculated osmolality (Δ osmolality) was used to calculate the ethanol concentration that would account for the increased serum osmolality: 3.0 g/liter. The measured ethanol concentration was only 1.86 g/liter, suggesting the possibility that there was another alcohol present, that the enzymatic ethanol determination was in error because of its lack of specificity, or that there might be another cause for the increased osmolality. Thus we did a gas-chromatographic analysis of the patient's serum and gastric contents. Figure 1 shows the resulting chromatogram for the patient's serum. Ethanol, acetone, and isopropanol were present and were quantitated in both serum and gastric contents: 0.90, 0.18, 1.65 g/liter and 3.12, 0.31, 5.34 g/liter for serum and gastric contents, respectively.

The patient was taken off the respirator and extubated the next day and was discharged two days later.

Discussion

This patient presumably had ingested some type of lotion (isopropanol) and ethanol. Using an enzymatic (alcohol dehydrogenase) procedure for ethanol gave an analytical result that was erroneous because the method is not specific for ethanol. Although both isopropanol and n-propanol cross react, they will be underestimated. For example, isopropanol, ingested alone, would be underestimated and methanol ingestion not detected. By measuring serum osmolality and performing a Δ osmolality calculation (1, 3) the presence of other alcohols was indicated and was confirmed by gas chromatography. The determination of the presence of other alcohols is important for the treatment of the comatose patient, because other causes of coma might also be present and must be excluded. In this case, the presence of other drugs was excluded and the coma was most likely attributable to the presence of ethanol and iso-

propanol, which also could account for the patient's symptoms. Isopropanol is twice as potent as ethanol, its systemic effects being similar to those of ethanol. It readily produces coma, which rarely lasts longer than 12 h in nonfatal cases (4). The serum isopropanol concentration in this patient was 1.65 g/liter the ethanol concentration 0.90 g/liter, a concentration near that legally defined as "under the influence of alcohol," which is 1.00 g/liter, would not by itself account for the patient's coma. However, the concomitant presence of 1.65 of isopropanol per liter in serum was the evident cause of the patient's coma. The fact that the acetone concentration in serum was so low (0.18 g/liter) indicates that the patient was seen soon after ingestion, because little of the isopropanol had been metabolized to acetone. Moreover, the ethanol and isopropanol present in the gastric contents (3.12 and 5.34 g/liter) indicated that the alcohols had not been completely absorbed.

Some cases of isopropanol ingestion resulting in coma and death have been reported (5, 6, 7). Serum isopropanol concentrations of 1.50 g/liter have been reported to result in coma in patients who misused isopropanol (7, 8). In other reports an isopropanol concentration of 1.5 g/liter of blood was found in fatal poisonings (5). The discrepancy between these reports is probably attributable to individual tolerance to isopropanol. Individuals with a tolerance for ethanol also have a tolerance for isopropanol. Our patient was in deep coma, which is consistent with the reported cases of isopropanol ingestion resulting in coma but not death (7, 8). Although the patient had a history of alcohol consumption, and thus probably had a tolerance to ethanol and isopropanol, emergency treatment and supporting therapy were also important in his recovery.

It is very important for the laboratory to be able to

Fig. 1. Gas–liquid chromatogram of the patient's serum
A, ethanol, 0.90 g/liter; B, acetone, 0.18 g/liter; C, isopropanol, 1.65 g/liter; D, n-propanol (internal standard), 1.00 g/liter. Conditions: Stainless-steel column, 1.8 m X 3 mm (i.d.), Porapak Q 80/100, nitrogen carrier gas, 20 ml/min. Column temp., 142 °C. Attenuation: 1 X 8. (See reference 1 for further details)
identify and separate the commonly misused alcohols. Because the enzymatic (AD) method for ethanol determinations may give erroneous results, all positive results by this method should be checked by another method. The data should be evaluated by comparison with the osmolality, and if there is a discrepancy the possibility that another alcohol is present should be considered and evaluated by another procedure such as gas chromatography.

References