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SHORT COMMUNICATION

False-positive breath-alcohol test after a ketogenic diet

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A 59-year-old man undergoing weight loss with very low calorie diets (VLCD) attempted to drive a car, which was fitted with an alcohol ignition interlock device, but the vehicle failed to start. Because the man was a teetotaller, he was surprised and upset by this result. VLCD treatment leads to ketonemia with high concentrations of acetone, acetoacetate and β-hydroxybutyrate in the blood. The interlock device determines alcohol (ethanol) in breath by electrochemical oxidation, but acetone does not undergo oxidation with this detector. However, under certain circumstances acetone is reduced in the body to isopropanol by hepatic alcohol dehydrogenase (ADH). The ignition interlock device responds to other alcohols (e.g. methanol, n-propanol and isopropanol), which therefore explains the false-positive result. This 'side effect' of ketogenic diets needs further discussion by authorities when people engaged in safety-sensitive work (e.g. bus drivers and airline pilots) submit to random breath-alcohol tests.
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Obesity constitutes a serious threat to health and longevity and among various treatment options, very low calorie diets (VLCD) are frequently used.[1,2] Such diets provide essential proteins and fats but negligible amounts of carbohydrates and they typically furnish 800 kcal/day. After a few days of dieting, fat becomes the main source of energy, and VLCD regimens are consequently ketogenic.[3]

Ketone bodies (acetone, acetoacetate and β-hydroxybutyrate) increase appreciably in the blood of people on VLCD.[4,5] Acetone is a water-soluble volatile product of metabolism and is therefore exhaled in the breath and excreted in the urine. Indeed, monitoring breath-acetone has been advocated as a way to ensure that patients comply with their VLCD treatment.[5]

The elimination half-life of acetone in man is fairly long (15–25 h) and the biosynthesis and metabolic fate of this endogenous metabolite are summarized in Figure 1.[6,7] During ketonemia, the reduction pathway toward isopropanol becomes a strong possibility and, indeed, this secondary alcohol has been identified in blood of patients with hyperglycemia and poorly controlled diabetes.[8–10] The conversion of acetoacetate into β-hydroxybutyrate and the reduction of acetone to isopropanol are both nicotinamide adenine dinucleotide (NAD)-dependent redox reactions.[7] Moreover, administration of amino acids, precursors of proteins, can accelerate the elimination of ethanol from blood by enhancing activity of hepatic alcohol dehydrogenase (ADH).[11] An increased ADH activity after eating high protein diets might help to promote reduction of acetone to isopropanol.

Among various strategies to reduce drunk driving and improve road traffic safety, the use of alcohol ignition interlock devices shows great promise.[12] Such devices are increasingly being fitted to buses and other public transportation vehicles as well as long-haul trucks and also in some private cars, especially in Sweden.[13] Incentives to install ignition interlock systems in private cars include lower insurance costs and earlier return of the driving permit to people convicted of drunk driving and especially to control recidivism.[12,13]

Most of the ignition interlock devices used today measure alcohol (ethanol) in a person's breath by electrochemical oxidation. Endogenous breath volatiles like acetone are not oxidized at the same electrode potential.[14] However, the secondary alcohol isopropanol (2-propanol) is oxidized at a slightly faster rate than ethanol and these two alcohols cannot be distinguished.[14] Accordingly, if acetone is reduced to isopropanol during ketonemia, there is a strong possibility of false-positive results when ignition interlocks are used. Indeed, the concentration threshold for a positive test and

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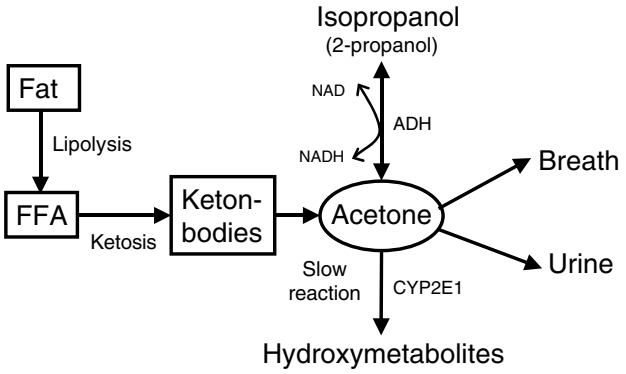

Figure 1 Biosynthesis and metabolic fate of acetone after ketogenic diets. FFA = free fatty acids; ADH = alcohol dehydrogenase; NAD^+ and NADH are oxidized and reduced forms, respectively, of the coenzyme nicotinamide adenine dinucleotide; CYP2E1 = cytochrome P450 isozyme.

failure to start the engine is often set fairly low, corresponding to a blood alcohol concentration (BAC) of 0.01–0.02 g/100 ml (10–20 mg/100 ml).

We report a case of a 59-year-old man, body mass index 26.6 kg/m^2, who began a weight reduction program, partly because of knee pains but also because he was a glider pilot where weight is important. He used a Swedish textbook on obesity treatment written by S Rössner together with the commonly used Swedish VLCD Nutrilett (Cederroths, Stockholm, Sweden), 5 packets/day for 3 weeks, which is an approved standard regimen. This treatment resulted in a weight loss of 7 kg.

During dieting, the man discovered that an alcohol ignition interlock device, installed in an official company car, indicated that he had consumed alcohol and the vehicle failed to start. This was confusing because the man was a lifelong teetotaller and was therefore both surprised and upset by the result. As he had been supervising private aviation he had access to a second breath-alcohol analyzer, which indicated a simultaneous BAC ranging from 0.01 to 0.02 g/100 ml.

In an attempt to understand the reason for the positive breath-test result, which obviously caused some discomfort and practical problems, the man contacted the Obesity Unit (Karolinska University Hospital, Stockholm, Sweden) for advice, and the mechanism was elucidated. Although we did not have the opportunity to measure acetone and isopropanol directly in this subject, the most plausible explanation for the positive breath-alcohol test is reduction of acetone to isopropanol, which then undergoes electrochemical oxidation.[10]

Most countries enforce statutory BAC limits above which it is an offence to drive a motor vehicle. These limits differ between countries owing to tradition, lifestyle and political influences.[15] The punishable BAC limits for driving range from as low as 0.02 g/100 ml in Norway and Sweden to 0.05 g/100 ml in most European countries and 0.08 g/100 ml in UK, Ireland, USA and Canada. It seems important therefore to consider the consequences of ketogenic diets when blood- and breath-alcohol tests are interpreted in a legal context.

Suspected drunk drivers first submit to a roadside breath-alcohol screening test and if this is positive they provide either an evidential breath-alcohol test or a blood specimen is taken for laboratory analysis. Breath-alcohol screening tests incorporate electrochemical detectors similar to those used in the ignition interlock device and therefore respond to isopropanol. By contrast, most evidential breath-testing is performed by multifilter infrared analysis and these are programmed to abort the test if acetone is detected on the suspect's breath above a certain threshold value.[10] Because the half-life of isopropanol ($t_{\frac{1}{2}}$ = 3–5 h) is much shorter than that of acetone ($t_{\frac{1}{2}}$ = 15–25 h), it is hard to envisage finding elevated concentrations of isopropanol without concomitant high concentrations of acetone. However, evidential breath-alcohol analyzers based on electrochemical oxidation cannot distinguish ethanol from isopropanol and this resulted in a false-positive test after VLCD. An apparent BAC of 0.02 g/100 ml seems likely according to the present case report.

The reduction of acetone to isopropanol is not a problem with blood-ethanol determination because gas chromatography is used and this highly specific method can resolve ethanol from both acetone and isopropanol under normal operating conditions.[15]

In conclusion, we suggest that people on ketogenic diets run the risk of false-positive breath alcohol tests owing to reduction of acetone to isopropanol. People on VLCD need to be warned about this artifact when alcohol ignition interlock devices are used. This possibility also warrants consideration in connection with workplace alcohol testing and screening of drunk drivers with electrochemical sensors. Both the manufacturers of ignition interlock devices and government agencies that monitor performance and administer sanctions should consider these problem. Technological improvements might be possible, for example, by measuring not only the final reading but also the kinetics of the detector response to different alcohols.

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