Impact of Water-Induced Diuresis on Excretion Profiles of Ethanol, Urinary Creatinine, and Urinary Osmolality

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Abstract

This article reports the impact of diuresis on urinary excretion of ethanol in seven healthy volunteers who drank 1000 mL of export beer (44 g ethanol) in 30 min and, 120 min later, ingested 500 or 1000 mL of water within 5 min. Urine was voided before drinking started and every 30–60 min for 360 min after the start of drinking. The concentration of ethanol in urine (UAC) was determined by headspace gas chromatography, the creatinine content was determined by Jaffe’s method, and osmolality was measured by freezing point depression. Maximum diuresis coincided with the peak UAC and was reached 60–90 min after the end of drinking. The urinary creatinine and osmolality dropped appreciably after drinking beer, and the lowest values coincided with peak diuresis. Creatinine was < 0.2 g/L in 22% of urine specimens, and osmolality was < 200 mOsm/kg in 31% of specimens. Production of urine decreased as UAC entered the postabsorptive phase but increased again after the subjects drank water 120 min after alcohol consumption. The amount of ethanol recovered in urine was 681 mg (standard deviation [SD] 203 mg) corresponding to 1.5% (SD 0.46%) of the dose administered. The concentrations of ethanol in successive voids during the postabsorptive phase were not influenced after subjects drank 500 or 1000 mL of water although diuresis increased and urinary creatinine and osmolality decreased. Measuring UAC provides a reliable way to monitor recent drinking, and unlike the analysis of illicit drugs in urine, the concentrations of ethanol are not influenced by diuresis.

Introduction

Measuring the concentration of ethanol in urine presents no analytical difficulties, and with the aid of gas chromatographic (GC) or immunoassay methods, accurate and precise results are obtained (1–5). However, care is necessary when the concentrations of ethanol in urine are interpreted, especially if the aim is to estimate the person’s co-existing blood-ethanol concentration (BAC) or to furnish evidence of alcohol-induced impairment (6,7). Some of the difficulties interpreting UAC, at least in part, stem from an erroneous comparison of the pharmacokinetics of ethanol with aspects of urine testing for illicit drugs of abuse (8–10).

The aim of this study was to investigate the influence of drinking water during the postabsorptive phase of ethanol pharmacokinetics on the excretion profile of ethanol and on the associated changes in urinary creatinine and osmolality, both of which are widely used markers for highly dilute specimens (11). The magnitude of ethanol-induced and water-induced diuresis was determined along with the fraction of the dose of ethanol recovered in the urine.

Material and Methods

Healthy male (n = 5) and female (n = 2) volunteers, all social drinkers, with a mean age of 36 years (standard deviation [SD] 11 years) and mean body weight of 80 kg (SD 10 kg), participated in a controlled experiment. In two male subjects, the experiment was repeated twice to investigate within-subject reproducibility. The study protocol was approved by the ethical review committee at the University Hospital in Linköping, and the subjects gave verbal consent.

All participants were required to abstain from drinking alcohol for 24 h before the experiment began, and alcohol-free status was confirmed by breath-alcohol analysis with an Alcolmeter S-D2 instrument (Lion Laboratories, Barry, Wales, U.K.). After making an initial urinary void, the subjects were required to consume 1000 mL of export beer (44 g ethanol), corresponding to 0.55 g ethanol per kilogram mean body weight, in exactly 30 min. Specimens of urine were then voided at 30, 60, 90, 120, 150, 180, 210, 240, 300, and 360 min after finishing the beer. The subjects were encouraged to empty the bladder completely each time urine was voided. The specimens were collected into a measuring cylinder, and the volumes were recorded to the nearest 2 mL. At 120 min postdrinking (150 min from start), the subjects were required to drink either 500 or 1000 mL of tap water, and urine specimens were again collected at exactly timed intervals as indicated.
The concentration of ethanol in urine was determined by headspace GC, which had a limit of detection of 0.01 g/L (12). Urinary creatinine was determined by the Jaffe method on a Hitachi 717 analyzer (13), and osmolality was measured at the hospital clinical chemistry laboratory by a method based on depression of the freezing point (14). Concentration-time profiles of ethanol as well as changes in creatinine and osmolality were plotted for each subject, and average curves and between-subject variation were calculated. The amount of ethanol excreted in urine was determined as the product of concentration and volume voided at each sampling time. Diuresis was reported as the volume of urine produced per minute at each sampling time.

Results

Figure 1 presents an example of the concentration-time profiles of ethanol in urine, the magnitude of diuresis, and changes in urinary creatinine and osmolality in one male subject considered representative of the group. Figure 2 shows the average curves for all seven subjects.

These graphs show that the concentration of ethanol in urine increased fairly rapidly after drinking the beer with a mean peak UAC of 0.70 g/L (SD 0.16 g/L) and a range from 0.51 to 0.98 g/L. The peak ethanol concentration was reached at 60 min after the end of drinking the alcohol or 90 min after the start of drinking. Ethanol-induced diuresis was most pronounced during the absorption portions of the curves with a mean of 11.4 mL/min (SD 4 mL/min) and ranging from 4.7 to 16.6 mL/min. After the peak UAC was reached, the production of urine decreased until the subjects drank water at 150 min timed from start of drinking. The maximum water-induced diuresis was 4.7 mL/min (range 0.66–6.8 mL/min) and occurred at 60 min after the drink was finished. Water-induced diuresis was less pronounced than alcohol-induced diuresis. The total quantity of alcohol recovered in the urine was only 681 mg (SD 203 mg), corresponding to 1.5% (SD 0.46%) of the 44 g administered.

The shape of the excretion profile of ethanol during the postabsorptive phase from 150 min after drinking and later was hardly influenced at all after the subjects drank 500 or 1000 mL of water (Figures 1 and 2). Despite the increased volume of urine produced, the concentration-time course of ethanol in five successive voids after drinking the water remained on the decline expected for zero-order elimination kinetics of ethanol.

The creatinine content of urine and the osmolality decreased
abruptly after the subjects drank beer, thereafter increasing again before the subjects drank water at 150 min (Figures 1 and 2). Figure 3 shows that creatinine content of urine and osmolality were highly correlated ($r = 0.86, p < 0.001$). Moreover, urinary creatinine and osmolality decreased exponentially as diuresis increased (Figure 4). The creatinine content of urine was < 0.20 g/L in 22% of specimens, and osmolality was < 200 mOsm/kg in 31% of specimens.

**Discussion**

After drinking beer, wine, or spirits, the ethanol contained in these beverages mixes completely with total body water (TBW) after the absorption process is complete. Indeed, ethanol dilution can be used to estimate TBW, and the results agree well with isotope-dilution and anthropometric methods (15). The production of urine increased appreciably after drinking beer because of the combined influences of water-induced and ethanol-induced diuresis, as expected. The diuretic action of ethanol is caused by inhibition of the secretion of antidiuretic hormone vasopressin from the posterior pituitary gland (16). The production of highly dilute urine was confirmed by a sharp drop in both creatinine content and osmolality, and a large number of specimens were below the threshold values accepted in urine-drug testing programs to spot highly dilute specimens (11). The peak diuresis was observed at 90 min after starting to drink beer and seemed to coincide with the lowest creatinine and osmolality values.

The concentration of ethanol in urine was highest at 90 min after the start of drinking, being followed by a more or less rectilinear declining phase until all the alcohol was eliminated after 6–7 h. The elimination profile of ethanol in urine seemed to follow a zero-order kinetics and the linear decline in UAC when the postabsorptive phase was well established was not disrupted after the subjects consumed 500 or 1000 mL of water 150 min from start of drinking (7, 15). Diuresis does not change the concentration of ethanol in urine even though creatinine content and osmolality were markedly reduced after drinking water. This supports an early observation made by Widmark (17, 18) and confirms that ethanol is excreted by the kidney according to a passive diffusion process (19–22). The concentration of ethanol in freshly produced urine reflects the concentration in the water fraction of blood flowing to the kidney, and this is not influenced by drinking 500 or 1000 mL of water (17, 18). The TBW is about 50–60% of body weight, and the concentration of ethanol in TBW is not markedly altered by intake of 500–1000 mL of water. The kidneys cannot produce ethanol at a greater concentration than that existing in the TBW (20, 21).

The fact that only 1–2% of the dose of ethanol administered was recovered in the urine confirms previous work on the disposition and fate of ethanol in the body (23). The normal production rate of urine in healthy adults is about 30–60 mL/h (720–1440 mL/day), and even increasing this volume by drinking copious amounts of water will have a minimal effect on the total amount of ethanol cleared by renal excretion. The differences in concentrations of ethanol between blood and urine depend mostly on the relative water content of the specimens analyzed and
also on the phase of ethanol metabolism when the samples are taken (24, 25). During the absorption phase shortly after the end of drinking, the BAC tends to exceed UAC, but when no more alcohol is consumed and equilibration of ethanol in all body fluids is complete, the UAC is, as expected, always higher than BAC because urine contains about 20% more water than an equal volume of whole blood (7, 25). The UAC/BAC ratio of ethanol for venous whole blood and freshly produced urine without long periods of storage in the bladder should be approximately 1.20:1. 

Because neither UAC nor BAC are seemingly lowered after drinking 500–1000 mL water, the urine/blood ratios of ethanol should also remain unchanged despite a marked water-induced diuresis. This is important to consider when the UAC/BAC ratio of ethanol is used to derive information about the likely time of consumption of alcohol in relation to sampling and also whether a person’s BAC might have been rising or falling some time prior to sampling (6, 7, 25). Urine is available in large volumes without invasion of the body and is widely used in analytical toxicology to monitor alcohol and drug abuse (26). The possibility of lowering the concentrations of illicit drugs in urine by drinking water prior to voiding is well known (27), but this strategy will not influence the concentration of ethanol in urine.

Several recent studies have explored the possibility of monitoring abstinence by the determination of ethanol in urine as a way to detect relapse in alcoholic outpatients or control for alcohol consumption in workplace accidents (28). Measuring UAC in the first morning void can disclose whether a person consumed alcohol the night before, and such information is useful to check for compliance with abstinence in addiction medicine (28, 29). Alcohol testing has proved a useful complement to personal interviews about the patient’s drinking habits. The first urinary void collected from a suspected drunk driver in traffic accidents in analytical toxicology to monitor alcohol and drug abuse (26). The possibility of lowering the concentrations of illicit drugs in urine by drinking water prior to voiding is well known (27), but this strategy will not influence the concentration of ethanol in urine.

In conclusion, measuring ethanol in urine has many applications in analytical toxicology and interpretation of urine results for ethanol is a lot easier than for other drugs of abuse. The UAC provides a useful way to monitor abstinence during rehabilitation programs for convicted drunk drivers and other public health activities where alcohol abuse is involved. Unlike urinalysis of many drugs of abuse (cannabis, amphetamine), the concentration of ethanol in the urine is not influenced by diuresis or the pH of the urine specimens. Drinking a large volume of water before voiding will not dilute the concentration of ethanol.

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References


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