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Reliability of Breath-Alcohol Analysis in Individuals with Gastroesophageal Reflux Disease*

ABSTRACT: Gastroesophageal reflux disease (GERD) is widespread in the population among all age groups and in both sexes. The reliability of breath alcohol analysis in subjects suffering from GERD is unknown. We investigated the relationship between breath-alcohol concentration (BrAC) and blood-alcohol concentration (BAC) in 5 male and 5 female subjects all suffering from severe gastroesophageal reflux disease and scheduled for antireflux surgery. Each subject served in two experiments in random order about 1–2 weeks apart. Both times they drank the same dose of ethanol (~0.3 g/kg) as either beer, white wine, or vodka mixed with orange juice before venous blood and end-expired breath samples were obtained at 5–10 min intervals for 4 h. An attempt was made to provoke gastroesophageal reflux in one of the drinking experiments by applying an abdominal compression belt. Blood-ethanol concentration was determined by headspace gas chromatography and breath-ethanol was measured with an electrochemical instrument (Alcolmeter SD-400) or a quantitative infrared analyzer (Data-Master). During the absorption of alcohol, which occurred during the first 90 min after the start of drinking, BrAC (mg/210 L) tended to be the same or higher than venous BAC (mg/dL). In the post-peak phase, the BAC always exceeded BrAC. Four of the 10 subjects definitely experienced gastric reflux during the study although this did not result in widely deviant BrAC readings compared with BAC when sampling occurred at 5-min intervals. We conclude that the risk of alcohol erupting from the stomach into the mouth owing to gastric reflux and falsely increasing the result of an evidential breath-alcohol test is highly improbable.

KEYWORDS: forensic science, alcohol, analysis, blood, breath-analysis, disease state, drinking and driving, DUI challenges, gastric reflux

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The use of breath alcohol testing has long traditions in clinical medicine, alcohol research, and especially in law enforcement practice as an indirect and non-invasive way of estimating a person's BAC (1–3). More recently, breath-tests for alcohol have been introduced and used for workplace alcohol testing, particularly in the transportation sector and other activities involving safety-sensitive work (4). Instead of translating breath-alcohol concentration (BrAC) into BAC, it has become customary to enforce threshold limits of BrAC, such as 0.10 and 0.08 g/210 L, which apply in most US States (5,6). In connection with workplace alcohol testing, the threshold limits of BrAC are set much lower, at 0.02 and 0.04 g/210 L (4).

Drunk driving laws in the US and most countries in Europe stipulate that the blood- or breath-alcohol concentration "per se" is the sole deciding factor for prosecution (3,6). This legal framework demands strict rules and regulations when evidential breath-alcohol tests are made including a mandatory 15 min observation period after the last drink to ensure that mouth-alcohol does not invalidate the results (2–4). The eruption of gastric contents (if these contain alcohol) into the throat and mouth owing to gastric reflux occurring immediately before or during the breath-test procedure might be argued would lead to a false high reading (7–10).

Gastroesophageal reflux disease (GERD) is regularly encountered in daily medical practice and symptoms include heartburn and sensations of retrosternal discomfort or burning that might extend upwards to the throat. eructation, and epigastric pain (11). The prevalence of GERD in the population is not known with certainty partly because many sufferers disregard mild symptoms of gastroesophageal reflux and do not seek medical treatment (11). It was reported that approximately 7% of US adults experience daily heartburn (12) so GERD probably represents a common disorder. even among those who might submit to a breath-alcohol test.

The aim of the present study was to assess the reliability of breath-alcohol analysis in patients diagnosed as chronic sufferers of GERD. We compared breath-alcohol concentrations with venous blood-alcohol concentrations in near simultaneous samples with the use of well established analytical methods for the determination of ethanol.

Methods

Patients and Conditions

Five male and five female subjects all with severe symptoms of GERD were recruited for the study after they had been referred to the University Hospital in Linköping for antireflux surgery. Medi-

cation with proton pump inhibitors (omeprazole or lansoprazole) was ineffective in relieving symptoms. All the patients underwent esophagogastric endoscopy, esophageal manometry, acid-reflux test (13) and pH was monitored for 24-h (14) before they were accepted for the drinking experiments. The study protocol was approved by the ethics committee at the University Hospital in Linköping, and all patients gave verbal consent.

Each subject took part in two experiments being randomly assigned to one of three groups depending on the kind of alcoholic beverage they were required to drink. Three subjects consumed 2 bottles (660 mL) export lager (5.2% vol/vol), three patients drank 2 glasses (300 mL) white wine (11.5% vol/vol) and the remaining four ingested 100 mL vodka (40% vol/vol) diluted with 200 mL pure orange juice. Demographic details of the patients, the kind of beverage and the amount of ethanol they consumed are summarized in Table 1. Two female subjects (GBP and ELJ) were given a slightly lower dose of alcohol because their body weights were 49 kg and 57 kg respectively.

After fasting overnight (10 h), the subjects arrived at the hospital at about 8.00 am and an intravenous catheter was inserted into a large cubital vein. The alcoholic drinks were presented at about 9.00 a.m. and they were finished in 15 min. Venous blood and end-expired breath were obtained before the start of drinking, at 10 min after drinking and then every 5 min for 2 h and finally at 10 min intervals for another 2 h.

Blood Sampling and Determination of Ethanol

Venous blood samples were obtained through an indwelling catheter with the subject resting in the supine position. The catheter tubing was flushed with a few drops of heparin-saline solution to prevent coagulation between taking successive samples. The blood was taken into 5 mL Vacutainer tubes containing NaF (20 mg) and heparin (143 units), and the tubes were stored at 4°C until analyzed about 24 h after sampling.

The BAC was determined in aliquots of venous whole blood (100 μL) by headspace gas chromatography as described in detail elsewhere (15). The limit of quantitation with this method was 1 mg/dL (0.2 mmol/L) under the conditions used. The coefficient of variation of blood-alcohol analysis at a mean BAC of 80 mg/dL (17.4 mmol/L) was less than 1%, indicating a high analytical precision (15).

Breath Alcohol Analysis

Immediately after the blood sample was drawn, each subject was required to provide a sample of breath by making a moderate inhalation and forced continuous exhalation for at least six seconds. Two kinds of breath-alcohol analyzer were used interchangeably. One device was an electrochemical analyzer (Alcolmeter SD-400), which provided a direct readout of BrAC in units of milligram alcohol per liter of breath, and the other was a quantitative infrared analyzer (DataMaster), which gave readings in units of g/210 L breath. With the DataMaster instrument, the entire exhalation profile was monitored on a computer interface from start to end of an exhalation and the highest BrAC reached was read from a digital display. In this article, the results of breath-alcohol testing are reported as mg/210 L breath, where 100 mg/210 L is the same as 0.10 g/210 L.[1]

The Alcolmeter SD-400 gave readings in units of mg alcohol per liter of breath to the nearest 0.01 mg/L. The standard deviation of a single measurement was 0.006 mg/L, corresponding to a coefficient of variation of 6% at a mean BrAC of 0.1 mg/L (unpublished work). Similarly, the DataMaster instrument produced readings in units of mg alcohol per 210 L breath and the coefficient of variation of a single determination was 3%.

Provocation of Gastric Reflux

In one of the two drinking experiments an attempt was made to provoke gastroesophageal reflux by applying an abdominal compression belt when the subject was resting in a supine position (16). The belt consisted of an inflatable rubber bladder measuring 25 cm by 40 cm, which was wrapped round the upper part of the abdomen. The pressure was raised to 50 mm Hg and this was maintained constant for 3 min by means of a manometer. This method has been shown to raise the intra-abdominal pressure by approximately 15 mm Hg (17). The belt was applied at approximately 27, 42, 62, 82, 102, and 122 min after start of ethanol administration. The maximal pressure was maintained for 3 min and during the last few seconds a venous blood sample was drawn. Immediately after deflating the pressure belt, each subject performed the breath-alcohol test.

[1] In the USA blood and breath-alcohol concentrations for legal purposes are reported as g/dL and g/210 L respectively.

TABLE 1.—*Demographic details of the subjects participating in the study, the alcoholic beverages they consumed, and the severity of gastroesophageal reflux.*

Subject/Sex*	Age (y)	Height (cm)	Weight (kg)	Drink	Ethanol (g)	Ethanol (g/kg)	LES† (mm Hg)	Total Reflux Time‡ (%)
KK/m	53	190	87	Beer	27.1	0.31	6	4.1
RB/m	56	170	73	Beer	27.1	0.37	15	15.9
GBP/f	44	152	49	Wine	19.5	0.39	2	16.2
JJ/m	44	177	80	Wine	27.2	0.34	7	1.6
KA/m	51	178	103	Vodka§	31.6	0.30	5	6.6
DM/m	52	172	92	Vodka§	31.6	0.34	9	4.3
ABA/f	56	165	86	Wine	27.2	0.31	1	11.1
HS/f	46	166	69	Beer	27.1	0.39	12	1.1
ELJ/f	28	160	57	Vodka§	25.2	0.44	6	2.5
PM/f	38	154	72	Vodka§	31.6	0.43	14	11.4

* m/f indicate male or female gender.
† LES indicates lower esophageal sphincter resting pressure during esophageal manometry.
‡ Total reflux time indicates fraction of total time with pH below 4 during conventional 24-h ambulatory pH monitoring.
§ Vodka (40% v/v) diluted with orange juice.

Pharmacokinetics

Blood ethanol- and breath ethanol profiles were plotted for each subject in both drinking sessions with and without provocation of reflux. From these profiles the peak concentration (C_{max}) and the time required to reach peak concentration (t_{max}) were noted and the areas under the curves (AUC_{145}) were determined by the linear trapezoidal rule from 0–145 min.

Statistical Analysis

Statistical significance of differences was assessed by use of the non-parametric Wilcoxon's signed-ranks test for paired observations (intra-individual differences) and $p < 0.05$ was considered statistically significant.

Results

All patients had a hiatal hernia and an incomplete closure of the gastroesophageal junction at endoscopy. During the acid reflux test, the results were considered positive if two pH readings below 4 were obtained. The mean lower esophageal sphincter (LES) resting pressure was 7.7 mm Hg (SD 4.8 mm Hg; Table 1). During the 24-h ambulatory pH measurement, reflux was considered to have occurred every time pH was below 4 and the mean fraction of total reflux time was 7.5% (Table 1).

Figures 1 and 2 show representative examples of blood and breath-alcohol profiles for four of the volunteer subjects (A-D) and their demographic details can be found in Table 1. For each plot, the control session is shown in the upper part and the corresponding lower frames show the results after applying an abdominal pressure belt at the times indicated by arrows and the words reflux provocation. Subject D complained of severe retrosternal pain and heartburn and therefore fewer attempts were made to provoke reflux in this individual. These graphs show that BrAC in some subjects tends to overstate venous BAC during the absorption phase of the curves, for the first 90 min after the end of drinking; the maximum deviation BrAC-BAC was 30 mg/210 L. At later times and for the remainder of the post-absorptive phase, BrAC understated venous BAC. These results confirm previous work and can be explained, at least in part, by arterial-venous differences in blood-alcohol concentrations (18,19). No unexpected or spurious increases in BrAC were observed after applying pressure to the abdomen even though replicate breath tests were made every 5 min and 4 of the 10 subjects complained of gastric reflux once or more during the study.

Table 2 compares the pharmacokinetic parameters C_{max}, t_{max} and AUC with and without provocation of reflux. No statistically significant differences were noted between blood- and breath parameters in the two test sessions ($p > 0.05$).

Discussion

Gastroesophageal reflux occurs when the intragastric pressure overcomes the competence of the gastroesophageal junction. The development of GERD is multifactorial and seems to be related to the effectiveness of the lower esophageal sphincter (LES) to act as a barrier against retrograde flow. The efficacy of esophageal clearance and gastric emptying are important in this respect (20). Environmental factors such as eating spicy foods, smoking, and various medicines can contribute to the impairment of the LES causing reflux to occur (21–23). In connection with breath-alcohol testing, it is noteworthy that drinking high-proof alcoholic beverages (23,24) as well as beer and white wine (25) also induce gastroesophageal reflux in some subjects.

All patients recruited for the present study had pronounced symptoms of reflux and some suffered from coughing, hoarseness,
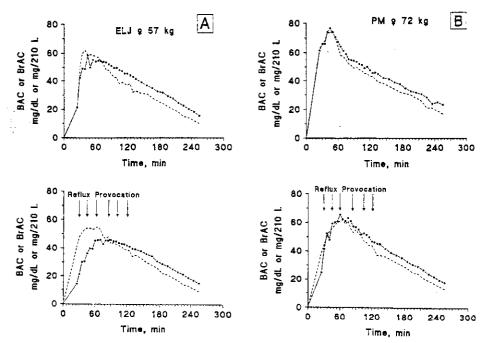

FIG. 1—*Blood (——) and breath (----) alcohol profiles in two subjects (A and B) who drank a moderate dose of alcohol (~0.3 g/kg) on an empty stomach. Near simultaneous samples of blood and breath were obtained at 5 min intervals for 2 h and then at 10 min intervals for another 2 h. The arrows mark the times when reflux was provoked by applying a pressure belt to the abdomen. For clarity, the symbols representing sampling times have been excluded from the breath-alcohol profiles.*
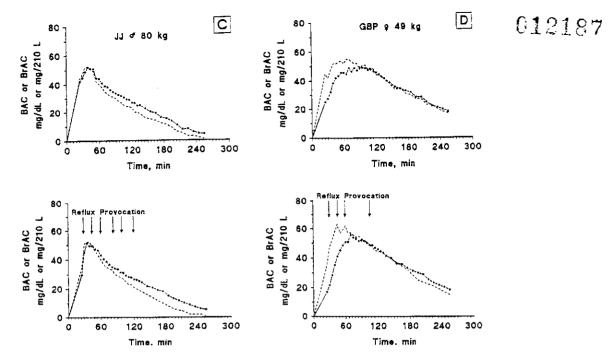
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FIG. 2—Blood (•—•) and breath (----) alcohol profiles in two subjects (C and D) who drank a moderate dose of alcohol (~0.3 g/kg) on an empty stomach. Near simultaneous samples of blood and breath were obtained at 5 min intervals for 2 h and then at 10 min intervals for another 2 h. The arrows mark the times when reflux was provoked by applying a pressure belt to the abdomen. For clarity, the symbols representing sampling times have been excluded from the breath-alcohol profiles.

TABLE 2—Blood-alcohol and breath-alcohol parameters (mean ± SD) for individuals suffering from gastroesophageal reflux disease (n = 10) after they had consumed alcoholic beverages equivalent to ~0.30 g/kg ethanol as beer, white wine or vodka mixed with orange juice.*

Conditions	Blood-Alcohol Profile	Breath-Alcohol Profile	P-value†
With reflux provocation			
C_{max} (mg/dL or mg/210 L)	53.6 ± 10.2	55.7 ± 7.1	0.58
t_{max} (min)	54.5 ± 19.1	42.0 ± 14.0	0.08
AUC_{145} (mg/dL × h or mg/210 L × h)	79.7 ± 16.4	83.8 ± 15.2	0.72
Without reflux provocation			
C_{max} (mg/dL or mg/210 L)	56.2 ± 13.2	58.0 ± 8.3	0.44
t_{max} (min)	47.5 ± 17.7	43.5 ± 11.6	0.13
AUC_{145} (mg/dL × h or mg/210 L × h)	86.4 ± 21.0	84.5 ± 20.8	0.77

* C_{max} indicates peak alcohol concentration; t_{max} is the time to reach peak blood or breath alcohol concentration after the start of drinking; AUC_{145} is the area under the curves from 0 to 145 min after the start of drinking.
† Non-parametric method for paired comparisons Wilcoxon's signed-ranks test.

and sore throat indicating extraesophageal complications (26). All subjects had a hiatal hernia, an abnormality which is frequently associated with GERD (20), they were resistant to conventional medication and were therefore scheduled for surgical intervention. Gastroesophageal reflux was documented by 24-h ambulatory pH monitoring, which is a highly sensitive and specific method (14), and generally considered to be the "gold standard" for documenting gastroesophageal reflux (26).

We feel confident that the patients participating in this study had well defined problems with gastroesophageal reflux even if it might be argued we did not objectively monitor reflux during the drinking experiments. Additionally, 4 of the 10 patients reported experiencing symptoms of reflux during the experiments indicating that gastric contents had erupted into the esophagus.

After drinking alcoholic beverages, the alcohol they contain is diluted with the contents of the stomach before entering the blood stream by a passive diffusion process (27). As absorption proceeds through the gut-wall, the concentration of alcohol in the stomach decreases exponentially (27,28). Gastric emptying increases the speed of alcohol absorption appreciably and the concentration in the stomach decrease more rapidly. About 90 min after the end of drinking, when the BAC-profile enters the post-absorptive phase, the concentration of alcohol in the stomach should be roughly the same as that in the peripheral venous blood. Accordingly, if gastric reflux occurred 90 min or more after the end of drinking it should not compromise the results of an evidential breath-alcohol test because the concentration of alcohol in the gastric fluid at this time is relatively low and probably similar to that of mucous secretions in

the mouth and upper-airway. Obviously, the risk of gastric reflux increasing the result of a breath-alcohol test will be greatest shortly after the end of drinking when the concentration of alcohol in the stomach is at its highest.

Early after the start of drinking when large amounts of alcohol are still unabsorbed in the stomach, BrAC (mg/210 L) was found to exceed BAC (mg/dL) because the arterial blood has a higher concentration of alcohol than the venous blood during the absorption portions of the curves (19). In the post-peak phase when arterial-venous differences in alcohol concentration are small or negligible, BAC (mg/dL) tends to exceed BrAC (mg/210 L). As discussed elsewhere, the magnitude of the differences between blood and breath-alcohol concentrations during different stages of ethanol metabolism depends to some extent on the way that BrAC is reported, e.g., whether as mg/200L, mg/210L, or mg/230L (19). However, most US states and the federal jurisdiction requires that breath-alcohol concentration is reported as g/210 L and blood-alcohol reported in units of g/dL, which corresponds to a BAC/BrAC ratio of 2100:1. But it should be noted that a fixed blood-to-breath relationship is not recognized by most laws and regulations (19).

The subjects who experienced gastric reflux in this study complained of unpleasant sensations in the throat, which proved incapacitating for short periods. Nevertheless, all patients were able to perform the breath-alcohol test shortly afterwards by making a moderate inhalation and forced deep exhalation. The differences between BAC and BrAC observed during different stages of the pharmacokinetics of ethanol did not seem to depend on whether or not reflux was provoked (Table 2).

To our knowledge, this is the first controlled investigation into the impact of gastroesophageal reflux disease on the reliability of breath-alcohol analysis. The results presented will be useful to rebut defense arguments that focus on GERD as a medical condition that might compromise the application of breath-alcohol instruments for workplace alcohol testing and in traffic law enforcement (29).

We conclude that the risk of a person experiencing gastric reflux during the time he or she participates in a breath-alcohol test procedure is very low. Even if reflux does occur, our study shows that it is not very likely that an abnormally high BrAC reading will be obtained. However, the mandatory 15 min observation period still remains an important element of the evidential breath-alcohol test protocol because this can help to rebut allegations that gastric reflux occurred. Likewise the routine practice of analyzing duplicate breath samples is an additional safeguard in this respect (30).

Acknowledgments

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