Pharmacology Biochemistry & Behavior, Vol. 22, pp. 811–814, 1985. © Ankho International Inc. Printed in the U.S.A. 0091-3057/85 $3.00 + .00

Acute Alcohol Intoxication and Body Composition in Women and Men

KENNETH C. GOIST, JR.*[1] AND PATRICIA B. SUTKER†

**Department of Psychiatry and Behavioral Sciences, Medical University of South Carolina, Charleston, SC and Department of Psychiatry and Neurology, Tulane University School of Medicine, New Orleans, LA*
†Department of Psychiatry and Neurology, Tulane University School of Medicine and Psychology Service, Veterans Administration Medical Center, New Orleans, LA

Received 26 September 1984

GOIST, K. C., JR. AND P. B. SUTKER. *Acute alcohol intoxication and body composition in women and men.* PHARMACOL BIOCHEM BEHAV 22(5) 811–814, 1985.—The present study was a direct experimental comparison of administering equivalent alcohol doses based on body weight and estimated total body water to 12 women and 12 men. Each subject participated in two experimental sessions separated by at least three days. Two doses of 95% ethanol were administered in a randomized, counterbalanced order: 0.66 ml/kg of body weight, and 1.2 ml/l of total body water. Women were tested during the midfollicular phase of their menstrual cycle when plasma concentrations of estrogen and progesterone have been found to be lower than other phases of the cycle. When given doses equated for body weight, women reached significantly higher peak blood alcohol concentrations than men. No sex differences were found when equivalent doses based on total body water were administered. This differential effect of dose determination was not reflected in self-reported levels of alcohol intoxication. The anthropometric equations used to estimate total body water provided a practical, reliable method for equating alcohol doses.

Acute intoxication Alcohol metabolism Blood alcohol concentration Body composition Body water Men Women

WHEN given equivalent alcohol doses based on body weight, women reach significantly higher blood alcohol concentrations (BACs) than men [1, 4, 5, 7, 12]. This sex difference in alcohol pharmacokinetics has been attributed to differences in the body composition of women and men [5, 7, 12]. Women are characterized by more fat and less body water per kg of body weight than men. Being more soluble in water than in other body constituents, alcohol is distributed primarily in the body water compartment [6]. Thus, women may reach significantly higher peak BACs than men because alcohol doses are distributed in smaller body water compartments. Two recent investigations found no sex differences when alcohol pharmacokinetic measures were adjusted statistically for total body water, estimated anthropometrically [12], or measured directly by ^{3}H-water dilution [7].

The present study is a direct experimental comparison of alcohol pharmacokinetics in women and men administered doses equated for body weight and total body water using a repeated measures design. In addition, the feasibility of applying simple anthropometric equations for estimating total body water as a reliable, practical method for calculating equivalent alcohol doses is explored.

METHOD

Subjects

Subjects were 12 women and 12 men recruited from staff employees of a large medical complex. All were volunteers who responded to advertisements placed on bulletin boards throughout the medical complex requesting participants for a psychological study and specifying compensation. Subjects ranged in age from 21–35 with a mean of 25.3±4.1 years. They reported an average daily consumption of 27.2±12.5 ml of absolute alcohol with a range of 12.0–47.7 ml/day. Their scores on the Shipley Institute of Living Scale ranged from 113.1–143.9 with a mean of 134.1±8.3. Women did not differ from men on the above personal characteristics (p's>0.10). Potential subjects were eliminated from study participation for the following self-reported reasons: (1) family history of alcoholism; (2) drinking more than twice the national average of 27.8 ml/day [9] or less than two times/week; (3) body fat composition of greater than 20%; (4) use of oral contraceptives; (5) history of menstrual irregularities or medical complications; and/or (6) pregnancy or expressed intent to become pregnant.

Apparatus and Instruments

Subject weight was determined using a Healthometer balance scale which provided measurements to the nearest 0.1 kg. BACs were determined from breath samples using an Intoximeter Model 3000. Subject perceptions of intoxication level were assessed using a 10-point self-rating scale with a score of 1 representing no intoxication and 10 representing extreme intoxication.

[1]Requests for reprints should be addressed to Kenneth C. Goist, Jr., PhD, Department of Psychiatry and Neurology, Tulane University School of Medicine, 1430 Tulane Ave., New Orleans, LA 70112.

Procedure

Subject screening procedures and instruments were identical to those reported previously [12]. Subjects who met the eligibility requirements reported to the laboratory at 8:00 a.m. on the morning of an experimental session after refraining from eating or drinking (except water) from 10 p.m. the night before and consuming no alcohol or drugs for 24 hours prior to a session. Women contacted the experimenters on the first day of their next menstrual cycle, and their first experimental session was scheduled for Days 5–7.

Each subject participated in two experimental sessions. The mean number of days between sessions was 3.6±1.2. Two doses of alcohol were administered in a randomized, counterbalanced order: 0.66 ml/kg of body weight, and 1.2 ml/l of total body water. Alcohol doses were selected based on data reported previously [12]. That is, the ratio of mean body weight to mean total body water for women and men was found to be 1.8. A dose based on total body water comparable to that based on body weight (0.66 ml/kg) was determined by multiplying this ratio of body weight to total body water by 0.66; the result was 1.2 ml/l of body water. Total body water was estimated using anthropometric equations [8] shown in Table 1. A mixture of 95% ethanol in a 1:4 ratio with decarbonated tonic water and a slice of lemon were used for both beverage preparations.

Experimental sessions were conducted according to procedures similar to those reported elsewhere [12]. Subjects drank the alcoholic beverage at a constant rate for 15 min, and breath samples were obtained at 5-min intervals until BACs were less than 15 mg/dl. Self-ratings of intoxication were recorded every 20 min until a rating of one (completely sober) was reported.

Alcohol pharmacokinetic measures and self-ratings of intoxication were analyzed by separate Ss/sex × dose determination ANOVAs. When the sex × dose determination interaction was significant, the simple main effects of sex were analyzed using Satterthwaite's [10] approximation for error degrees of freedom as recommended by Winer [14].

TABLE 1

ANTHROPOMETRIC EQUATIONS [8] USED TO ESTIMATE TOTAL BODY WATER (TBW) FROM BODY WEIGHT (BWT)

Women age 15–30	TBW=11.63 ± 0.318 (BWT)
Men age 16–30	TBW=13.26 ± 0.404 (BWT)

RESULTS

Peak BACs for women and men were differentially affected by the method of calculating alcohol dose. That is, whether the dose was based on body weight or estimated total body water significantly influenced peak BACs as evidenced by the sex × dose determination interaction (Table 2). Subsequent tests revealed that peak BACs for women were significantly lower for the dose determination based on estimated body water compared to that based on body weight, $F(1,22)=5.26$, $p=0.03$. Peak BACs for men did not differ across the two dose determination conditions, $F(1,22)=1.26$, $p=0.27$. When given equivalent doses based on body weight, women reached significantly higher peak BACs than men, $F(1,38)=4.47$, $p=0.05$. No differences in peak BACs were found between women and men when the dose was based on estimated total body water, $F(1,38)=0.43$, $p=0.53$. The main effects for sex and dose determination were not significant.

Similar results were obtained from analyses of the area under the BAC-time curves (AUCs) shown in Table 2. The AUCs were calculated from the actual BAC values, measured from the first valid BAC (5 minutes after the end of drinking) to 15 mg/dl or below, using the trapezoidal method. When administered doses equated for body weight, the AUCs for women were significantly larger than those for men, $F(1,32)=8.3$, $p=0.008$, but no differences were found when doses were equated for total body water, $F(1,32)=0.24$, $p=0.64$. Significantly larger AUCs were obtained for women administered the equivalent body weight dose compared to the total body water dose, $F(1,22)=10.74$, $p=0.003$. The AUCs for men did not differ significantly for the two dose determination conditions, $F(1,22)=3.98$, $p=0.06$. There were no significant main effects for sex or dose determination.

No differences were found for the time from the end of drinking to attainment of peak BAC for sex, dose determination or sex × dose determination interaction (Table 2). There was, however, a significant sex × dose determination interaction for the time from attainment of peak BAC to the end of the session (15 mg/dl or below). This interaction cannot be explained by differences between women and men when the dose was based on body weight, $F(1,29)=1.74$, $p=0.20$, or when it was based on body water, $F(1,29)=0.47$, $p=0.50$. No significant main effects for sex or dose determination were found for elimination time.

The total amount of alcohol administered for the two dose determination conditions did not differ, confirming the comparability of the doses chosen (Table 2). However, the sex × dose determination interaction was significant (Table 2). When administered the dose based on estimated body water compared to body weight, women received significantly less alcohol, $F(1,22)=17.64$, $p=0.0004$, and men received significantly more alcohol, $F(1,22)=25.62$, $p=0.00005$. The mean percentage of total body water for men (58.3%) was significantly greater than that for women (52.5%; $F(1,22)=45.25$, $p=0.00001$).

The apparent volume of distribution (V_D) was significantly greater overall for men than women (Table 2). V_D was estimated by dividing the total amount of alcohol administered by the derived BAC at the start of drinking (C_0). As shown in Fig. 1, the descending limbs of the BAC curves were nonlinear throughout. Therefore, C_0 was derived by extrapolating to time zero the nonlinear regression equation calculated from the descending limb of each BAC curve. The main effect for dose determination and the sex × dose determination interaction were not significant. The order in which the doses were administered had no effect on any of the alcohol pharmacokinetic measures (p's>0.05).

Differences in peak BACs for women and men as a function of the method for calculating doses were not reflected in self-ratings of intoxication reported at peak BAC, $F(1,22)=0.16$, $p=0.69$. In fact, the simple correlations between peak BACs and self-ratings of intoxication reported at peak BAC for all subjects were of little magnitude (body weight dose, r=.18 and total body water dose, r=.11). No differences in self-ratings were found between women and men, $F(1,22)=0.25$, $p=0.63$, or between the two dose determination conditions, $F(1,22)=0.63$, $p=0.43$.

TABLE 2

MEANS AND STANDARD DEVIATIONS FOR ALCOHOL PHARMACOKINETIC MEASURES

	Women (n=12)		Men (n=12)	
	Body Weight Dose (0.66 ml/kg)	Body Water Dose (1.2 ml/l)	Body Weight Dose (0.66 ml/kg)	Body Water Dose (1.2 ml/l)
Peak BAC* (mg/dl)	83.58 ± 12.06	75.75 ± 9.16	74.67 ± 9.9	78.50 ± 9.93§
AUC† (mg·5 min/ml)	11.7 ± 2.71	9.98 ± 1.91	9.33 ± 1.77	10.38 ± 1.44§
Time (min) to peak BAC	24.58 ± 13.73	25.42 ± 10.1	21.67 ± 10.3	22.92 ± 6.2
Time (min) from peak to 15 mg/dl	235.83 ± 25.48	220.42 ± 42.5	215.83 ± 44.41	230.83 ± 33.22§
Total amount (ml) of alcohol administered	37.76 ± 4.35	35.51 ± 2.55	49.44 ± 5.67	52.15 ± 4.12§¶
V_D‡	0.43 ± 0.09	0.40 ± 0.05	0.58 ± 0.11	0.57 ± 0.08¶

*Blood alcohol concentration.
†Area under the BAC-time curve.
‡Apparent volume of alcohol distribution.
§Significant sex × dose determination interaction (p's<0.03).
¶Significant sex effect (p's<0.01).

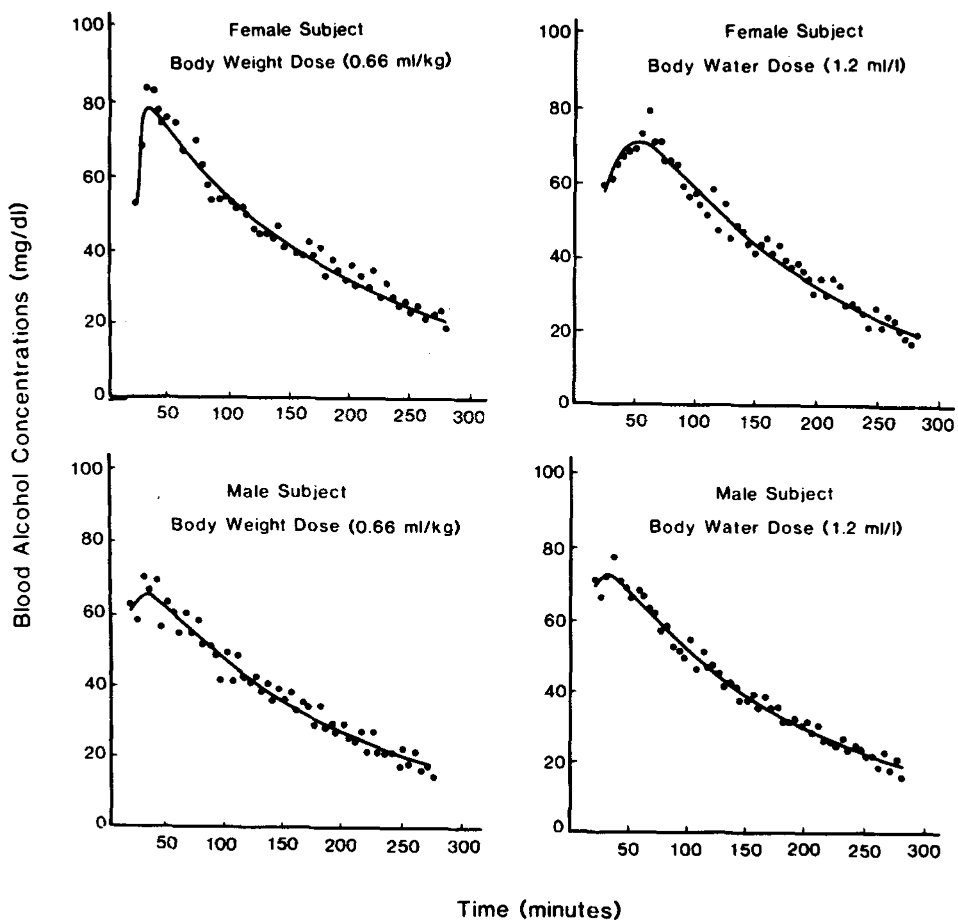

FIG. 1. BAC curves for a typical female (top) and male (bottom) subject given equivalent alcohol doses based on body weight (left) and estimated total body water (right). Lines were fitted to data points using nonlinear regression analyses.

DISCUSSION

The present study confirmed and extended earlier findings [7,12] that sex differences in alcohol pharmacokinetic measures were influenced significantly by differences in body composition. When administered alcohol doses based on body weight, women in the present study reached significantly higher peak BACs and showed larger AUCs than men, but no differences were found when the doses were equated for estimated total body water. A similar trend was discovered for elimination time, although comparisons between women and men for each dose determination condition revealed no differences. These alcohol pharmacokinetic measures varied systematically with the total amount of alcohol administered to women and men based on body weight and estimated total body water.

The differential effects of dose determination on elimination time found in this study are difficult to interpret in light of conflicting research reports of sex differences in elimination rates and times [1, 5, 7, 12]. This controversy may be attributed to the paucity of well-controlled studies investigating alcohol pharmacokinetics throughout the entire course of acute alcohol intoxication in women and men. The terminal portions of the BAC curve, despite their contribution of less than 5% of the total AUC [7], are necessary for accurate descriptions of alcohol elimination in terms of Michaelis-Menten kinetics [13].

Present findings show that anthropometric equations for estimating total body water may be used reliably to equate alcohol doses administered to women and men whose body weights are within the "normal" range. The mean percentages of total body water for women and men as calculated by the equations used in the present study are comparable to values obtained by direct measurement [7]. The accuracy of the equations is commensurate with those employing more complex anthropometric measures, although agreement is slightly greater for women [11]. An advantage of these equations is that only measurement of body weight is required, and thus no more information is needed to calculate alcohol doses than has been used traditionally.

Although women reached higher peak BACs than men when administered equivalent doses based on body weight, concomitant differences in self-ratings of intoxication were not observed. Other studies have shown an inverse relationship between BAC discrimination accuracy and absolute BAC values in social drinkers [2,3]. Therefore, multivariate and more precise assessment techniques are needed to determine whether the differential peak BACs found in women and men given equivalent doses based on body weight produce higher, pharmacologically effective doses of alcohol. Such studies should be extended from comparisons of socially drinking women and men to subjects in heavier drinking subgroups defined as "at risk" for alcohol abuse by familial history of alcoholism. The present study offers a useful paradigm for investigating these possibilities.

Additional research is needed to replicate and extend these preliminary findings, especially for administration of higher alcohol doses to various subgroups of drinking women and men. Calculation of doses based on total body water may also facilitate clarification of the discrepancies found in the literature concerning alcohol metabolism in women and its relationship to fluctuations of gonadal hormones across menstrual cycle phases. Further, relationships between total body water and acute and chronic intoxication across a broad range of age categories and racial groups require investigation.

ACKNOWLEDGEMENTS

This investigation was supported by the National Institute on Alcohol Abuse and Alcoholism, Research Grant No. RO1-AA05673 and Research Training Grant No. T32-AA07390, and was conducted within the Department of Psychiatry and Neurology, Tulane University School of Medicine, New Orleans, LA.

REFERENCES

1. Dubowski, K. M. Human pharmacokinetics of ethanol. I. Peak blood concentrations and elimination in male and female subjects. *Alcohol Tech Rep* **5**: 55–63, 1976.
2. Hay, W. M., P. E. Nathan, H. W. Heermans and W. Frankenstein. Menstrual cycle, tolerance and blood alcohol level discrimination ability. *Addict Behav* **9**: 67–77, 1984.
3. Huber, H., R. Karlin and P. E. Nathan. Blood alcohol level discrimination by nonalcoholics: The role of internal and external cues. *J Stud Alcohol* **37**: 27–39, 1976.
4. Jenkins, J. S. and J. Connolly. Adrenocortical response to ethanol in man. *Br Med J* **2**: 804–805, 1968.
5. Jones, B. M. and M. K. Jones. Alcohol effects in women during the menstrual cycle. *Ann NY Acad Sci* **273**: 576–587, 1976.
6. Kalant, H. Absorption, diffusion, distribution and elimination of ethanol. In: *The Biology of Alcoholism,* edited by B. Kissin and H. Begleiter. New York: Plenum Press, 1971, pp. 1–62.
7. Marshall, A. W., D. Kingstone, M. Boss and M. Y. Morgan. Ethanol elimination in males and females: Relationship to menstrual cycle and body composition. *Hepatology* **3**: 701–706, 1983.
8. Moore, F. D., K. H. Olson, J. D. McMurrey, H. V. Parker, M. R. Ball and C. M. Boyden. *The Body Cell Mass and Its Supporting Environment.* Philadelphia, PA: Saunders and Co., 1965.
9. Noble, E. P., editor. *Third Special Report to the U.S. Congress on Alcohol and Health.* Rockville, MD: National Institute on Alcohol Abuse and Alcoholism, 1978.
10. Satterthwaite, F. E. An approximate distribution of estimates of variance components. *Biometrics Bull* **2**: 110–114, 1946.
11. Steinkamp, R. C., N. L. Cohen, W. R. Gaffey, T. McKey, G. Bron, W. E. Siri, T. W. Sargent and E. Isaacs. Measures of body fat and related factors in normal adults—II: A simple clinical method to estimate body fat and lean body mass. *J Chronic Dis* **18**: 1291–1307, 1965.
12. Sutker, P. B., B. Tabakoff, K. C. Goist, Jr. and C. L. Randall. Acute alcohol intoxication, mood states and alcohol metabolism in women and men. *Pharmacol Biochem Behav* **18**: 349–354, 1983.
13. Wagner, J. G., P. K. Wilkinson, A. J. Sedman, D. R. Kay and D. J. Weidler. Elimination of alcohol from the human blood. *J Pharm Sci* **65**: 152–154, 1976.
14. Winer, B. J. *Statistical Principles in Experimental Design,* 2nd edition. New York: McGraw-Hill Book Co., 1971.