

Acute Alcohol Intoxication in Women: Relationship to Dose and Menstrual Cycle Phase

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This study investigated relationships between metabolic responses to acute alcohol intoxication and phases of the female menstrual cycle among women demonstrated to have ovulated during two consecutive cycles. Subjects were administered moderate (0.66 ml/kg) and high (1.0 ml/kg) alcohol doses during the early follicular, ovulatory, and midluteal phases of the menstrual cycles. Radioimmunoassays (RIAs) of serum estradiol, progesterone, luteinizing hormone (LH), and follicle-stimulating hormone (FSH) levels were performed from blood collected before each alcohol administration. Results showed decreased elimination times, reduced areas under the BAC-time curve (AUCs), and faster disappearance rates associated with the midluteal menstrual phase compared to the early follicular and ovulatory phases which were consistent for both moderate and high alcohol doses. Decreased elimination times, smaller AUCs, and faster disappearance rates were associated with increased levels of progesterone, elevated progesterone to estradiol ratios, and decreased FSH levels. No differences were found in absorption time or peak BAC across phases of the menstrual cycle.

SEVERAL animal studies have suggested that sensitivity to alcohol in females is related to gonadal hormone levels. It has been reported that ovariectomized mice and rabbits were more sensitive to the pharmacologic actions of alcohol than were intact female animals and that this effect was attenuated by injection of exogenous estrogen.^{1,2} In another study, no differences were found in alcohol sensitivity of female mice as a function of ovariectomy or stage of the estrus cycle.³ However, Eriksson⁴ showed that voluntary consumption of a 10% v/v alcohol solution decreased among normal and ovariectomized rats administered synthetic estrogen. In humans, relationships between alcohol absorption and elimination and levels of gonadal hormones have been studied by within-groups comparisons of women across stages of the menstrual cycle and by comparisons of oral contraceptive users and nonusers. To date, this literature offers contradictory findings, as does that in animals.

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Jones and Jones⁵ found that women reached higher peak blood alcohol concentrations (BACs) when administered alcohol during the premenstrual (day 28) compared to the menstrual (day 1) and ovulatory (around day 14) phases. Comparing alcohol absorption and elimination rates between oral contraceptive users and nonusers during menstrual (days 1-3), intermenstrual (days 13-15), and premenstrual (days 26-28) phases, Jones and Jones⁶ reported no differences in alcohol absorption and elimination; however, women maintained on oral contraceptives metabolized alcohol slower than women not taking the pill. In another study, comparisons of oral contraceptive users and nonusers revealed that women maintained on oral contraceptives were characterized by slower alcohol elimination rates, longer intoxication times, slower disappearance rates, and lower peak BACs than nonusers.⁷

Extending this research with a more carefully controlled design, Zeiner and Kegg⁸ tested users and nonusers of oral contraceptives during menstruation (day 1) and midluteal (day 24) phases of the menstrual cycle and found that both groups reached lower peak BACs and showed slower elimination rates during the midluteal phase compared to menstruation. Users were also characterized by slower elimination rates and lower peak BACs than nonusers during the midluteal phase, but no group differences were found during menstruation. Comparisons of oral contraceptive users tested once during the period of pill consumption (days 6-25) and nonusers tested during the follicular phase (days 1-10), however, revealed no differences on alcohol pharmacokinetic measures, but contraceptive users did exhibit significantly higher acetaldehyde (ACH) levels than did nonusers.⁹ Using a similar moderate dose of alcohol, Marshall, Kingstone, Boss, and Morgan¹⁰ failed to find differences in alcohol absorption and elimination among women demonstrated to be normally cycling and tested during the midfollicular (days 8-10) and midluteal (days 22-24) phases.

One of the problems in interpreting results of these studies is the failure of investigators to determine serum estradiol and progesterone levels at the time of alcohol intoxication. For the most part, women have been assumed to be normally cycling or to have ovulated during the menstrual cycle under scrutiny, because basal body temperature (BBT) data were monitored. With the exception of the Marshall et al.¹⁰ study, ovulation was not confirmed by radioimmunoassay (RIA) of progesterone levels, and gonadal hormone levels were not assessed prior

to alcohol administration. Verification of fluctuations of gonadal hormones associated with ovulation may be seen to be important, because studies have shown that 20–25% of a given sample of female subjects may be characterized by anovulatory cycles.^{11,12}

This study examined relationships between menstrual cycle phase and alcohol absorption and elimination among women demonstrated to be normally cycling and ovulating during the cycles under scrutiny. The design represented a factorial combination of moderate and high alcohol doses and three points in the menstrual cycle. Two doses were administered, because studies have not examined whether intraindividual differences in alcohol pharmacokinetics vary by dose across menstrual cycle phases. Three phases were selected to allow sampling across discrete points in the cycle which differ significantly in hormonal activity. These included the early follicular (days 2–7), ovulatory (around day 14), and midluteal (days 20–25) phases. An additional purpose of the study was to correlate alcohol pharmacokinetic measures with gonadal and hypothalamic hormone levels determined by RIA.

MATERIALS AND METHODS

Subjects

Subjects were 16 Caucasian women recruited from staff and graduate student employees within a large medical complex. They were volunteers who responded to advertisements placed on bulletin boards throughout the complex requesting participants for a psychological study and specifying compensation. Women ranged in age from 21–31, with a mean of 26.3 ± 3.0 years. They reported an average daily consumption of 25.0 ± 8.9 ml of absolute alcohol. Most of the women were college educated. Eighty-eight potential subjects were interviewed individually to determine study eligibility, and 72 were excluded from participation. The following represented exclusion criteria: family history of alcoholism; drinking practices of more than 1.5 times the national average of 27.8 ml/day;¹³ or less than two times/week; body fat composition of greater than 20%; oral contraceptive use; history of menstrual irregularities or medical complications; and/or pregnancy or expressed intent to become pregnant.

Procedures

On initial contact, subjects were scheduled for individual screening sessions and were administered the Khavari Alcohol Test¹⁴ to quantify drinking experiences and history and health/menstrual history questionnaires. Body composition (% body fat) was calculated using the equations of Moore, Olson, McMurrey, Parker, Ball, and Boyden.¹⁵ Those who met the stringent eligibility requirements were asked to read and sign informed consent agreements. Women were requested to participate in six experimental sessions spaced over two consecutive menstrual cycles, to record alcohol consumption data for one complete menstrual cycle prior to beginning the experimental sessions, and to monitor BBT data during the entire three menstrual cycles constituting their experimental participation. Upon completion of the initial charting cycle, subjects were assigned randomly to one of three starting points corresponding with the three phases of the menstrual cycle specified for investigation. That is, one-third of the women began their experimental sessions at each of the three phases. The order for administration of the moderate and high alcohol doses was also randomized.

Selected menstrual cycle phases allowed sampling across discrete time points characterized by presumed significant changes in gonadal hor-

mone activity. However, there were additional reasons for deciding upon the specific time points. Characterized by low levels of gonadal hormone activity, the early follicular phase (days 2–7) was chosen, because normally cycling, socially drinking women have reported increased alcohol consumption to relieve tension and depression at this time.¹⁶ Women were tested around ovulation (day 14) when surges of luteinizing hormone (LH), follicle-stimulating hormone (FSH), and estradiol occur,¹⁷ because Jones and Jones⁵ reported lessened effects of intoxication at ovulation. Associated with relatively high levels of estradiol and progesterone, the midluteal phase (days 20–25) was selected, because conflicting results have been reported among women tested at this time.^{8,10} Focus on the midluteal phase also avoided those days possibly characterized by premenstrual syndrome (PMS) and hypothesized psychological and physical discomfort.

Subjects refrained from alcohol and drug consumption for 24 hr prior to the experimental sessions and from eating or drinking (except water) for 10 hr before participation. All experimental sessions were scheduled for 8:00 AM. Upon their arrival at the laboratory, women were weighed and questioned regarding food, beverage, and drug consumption compliance. Before alcohol administration, 15 cc of blood were drawn for RIAs described below. Moderate (0.66 ml/kg) and high (1.0 ml/kg) doses of alcohol were prepared in a 1:4 ratio with decarbonated tonic water and a slice of lemon by one experimenter, while a second experimenter conducted the experimental session. Equal amounts of the beverage were poured into three (moderate dose) or four (high dose) cups, and subjects were allowed 15 (moderate dose) or 20 (high dose) min to consume the beverage at a constant rate. At the end of drinking, subjects gargled and rinsed their mouths thoroughly to remove residual alcohol. Breath samples were obtained at 5-min intervals throughout the session until a BAC of 15 mg/dl or less was reached.

Radioimmunoassays

The second antibody method was used for performing RIAs with standards, samples, and controls run in duplicate. Standard ¹²⁵I kits from Cambridge Medical Diagnostic were used for RIAs of LH, FSH, and progesterone, and the Pantex immunodirect¹²⁵I kit was used for estradiol. Ranges for the standard curves were established as follows: estradiol—10–2560 pg/ml; progesterone—0.1–40 ng/ml, calibrated against the MRC Reference Preparation; LH—4–300 MIU/ml, calibrated against the First International Reference Preparation (WHO, 1974, 68/40); and FSH—3–200 MIU/ml, calibrated against LER 970 in ng/ml and then converted to MIU/ml according to the IRP HMG. The first antiserum, all generated in rabbit, cross reacted as follows: estradiol, 100% with β -E₂, 1.4% with α -E₂, and less than 0.018% with estriol; progesterone, 100% with progesterone; LH, 100% with LH and 6.7% with FSH; and FSH (antiserum 210 N), 100% with FSH and 0.3% with LH. Recovery of known amounts of estradiol, progesterone, LH, and FSH added to human serum was 99–103%, 106–115%, 97.4–98.7%, and 116%, respectively.

Statistical Analyses

Four of the 16 women who began study participation failed to complete the six experimental sessions by voluntarily withdrawing from the study. Eight of the remaining 12 women were judged to have ovulated during both cycles, based on evaluation of BBT data and serum levels of estradiol, LH, and FSH at ovulation and progesterone during the midluteal phase. Statistical analyses were performed on the data collected from the eight ovulatory women who completed six sessions. Multivariate analysis of variance (MANOVA: Ss \times Dose \times Menstrual Cycle Phase) was used to examine five pharmacokinetic variables: (1) absorption time, interval between the end of drinking and peak BAC; (2) peak BAC, highest BAC recorded; (3) elimination time, interval from peak BAC to end of the session, 15 mg/dl or less; (4) area under the BAC-time curve (AUC), calculated from actual BACs using the trapezoidal method; and (5) disappearance rate, calculated from the slope of the linear portion of

the descending limb of the BAC-time curve multiplied by 60 to reflect the rate of change per hour (β_{60}). The apparent volume of distribution was calculated as the total amount of alcohol administered divided by C_0 where C_0 was the y -intercept derived from the nonlinear regression fit of the entire descending limb of the BAC-time curve. The same analyses were performed on serum estradiol, progesterone, LH, and FSH levels as well as the progesterone:estradiol ratio which was calculated by converting serum progesterone levels to pg/ml and dividing by serum estradiol levels. Insufficient serum could be extracted from samples drawn from two of the eight ovulatory women to assay LH and FSH levels in one session each; therefore, analyses of LH and FSH reflect data from six subjects.

RESULTS

Women demonstrated to be ovulatory across two consecutive cycles were found to differ significantly on measures of alcohol pharmacokinetics. Table 1 presents means and standard deviations for the five pharmacokinetic variables examined in the study. Univariate F tests revealed phase differences in elimination times, AUCs, and disappearance rates ($F_{2,14} = 9.29, 5.50$, and 9.32 , respectively, $p < 0.05$). Absorption times and peak BACs did not differ across the three cycle phases ($F_{2,14} = 0.33$ and 0.92 , respectively, $p > 0.05$). Comparisons performed post hoc showed significantly shorter elimination times during the midluteal phase compared with the average of the early follicular and ovulatory phases ($F_{2,14} = 7.69$, $p < 0.01$) with no differences between the follicular and ovulatory phases ($F_{2,14} = 1.60$, $p > 0.05$). AUCs were also significantly smaller ($F_{2,14} = 4.52$, $p < 0.05$) and disappearance rates significantly faster ($F_{2,14} = 8.38$, $p < 0.01$) during the midluteal phase compared with the average of the early follicular and ovulatory phases with no differences between the follicular and ovulatory phases ($F_{2,14} = 0.98$ and 0.95 , respectively, $p > 0.05$). The menstrual cycle phase at which women began their experimental sessions (follicular, $n = 3$; ovulatory, $n = 3$; and midluteal, $n = 2$) had no effect on these results ($p > 0.05$).

Although results indicated the expected differences in alcohol pharmacokinetics attributed to alcohol dose, dose had no influence on the pattern of significant findings for menstrual cycle phases described above. Univariate F tests showed significantly higher peak BACs, longer elimination times, and larger AUCs associated with the high as op-

posed to the moderate dose ($F_{1,7} = 514.54, 195.83$, and 350.34 , respectively, $p < 0.01$). No differences were found for absorption time or disappearance rate ($F_{1,7} = 2.80$ and 2.51 , respectively, $p > 0.05$). There was no dose \times menstrual cycle phase interaction for any of the five pharmacokinetic measures ($p > 0.05$). In addition, the apparent volume of alcohol distribution ($F_{2,14} = 0.02$) and estimated total body water¹⁵ ($F_{2,14} = 0.56$) did not differ across menstrual cycle phases ($p > 0.05$).

Serum gonadal and hypophyseal hormone levels were found to differ across menstrual cycle phases, and the means and standard deviations for the RIA data are presented in Table 2. Univariate F tests revealed significant changes in serum estradiol, progesterone, progesterone/estradiol ratio, and FSH levels across cycle phases ($F_{2,14} = 9.57, F_{2,14} = 25.51, F_{2,14} = 10.71$, and $F_{2,10} = 7.92$, respectively, $p < 0.01$), but no difference was found for LH levels ($F_{2,10} = 3.28$, $p > 0.05$). Post hoc comparisons of progesterone, progesterone/estradiol ratio, and FSH data showed significantly higher progesterone levels and progesterone/estradiol ratios and lower FSH levels during the midluteal phase compared with the average of the early follicular and ovulatory phases ($F_{2,14} = 24.47, F_{2,14} = 21.11$, and $F_{2,10} = 6.77$, respectively, $p < 0.01$). No differences in progesterone, progesterone/estradiol ratio, or FSH levels were found between the early follicular and ovulatory phases ($F_{2,14} = 1.04, F_{2,14} = 0.21$, and $F_{2,10} = 1.15$, respectively, $p > 0.05$). Comparisons of estradiol levels, conducted post hoc, revealed significantly higher serum levels for the average of the ovulatory and midluteal phases compared to the early follicular phase ($F_{2,14} = 9.51$, $p < 0.01$). No difference was found for estradiol levels at ovulation compared to the midluteal phase ($F_{2,14} = 0.06$, $p > 0.05$). Estradiol ($F_{1,7} = 0.05$), progesterone ($F_{1,5} = 2.52$), and LH ($F_{1,5} = 0.28$) levels did not differ between doses ($p > 0.05$), and there were no dose \times menstrual cycle phase interactions ($p > 0.05$).

Based on results of the post hoc comparisons of significant menstrual cycle phase differences, change scores were calculated from the difference between the midluteal phase and the average of the other two phases and from the moderate and high doses combined for elimination time, AUC, disappearance rate, progesterone, progesterone/es-

Table 1. Means and Standard Deviations for Pharmacokinetic Variables across Doses and Menstrual Cycle Phases

Pharmacokinetic variables	Dose	Early follicular phase	Ovulation	Midluteal phase
Absorption time (min)	Moderate	26.25 \pm 8.76	29.37 \pm 14.74	25.63 \pm 12.66
	High	29.13 \pm 15.26	33.13 \pm 17.31	34.37 \pm 14.74
Peak BAC (mg/dl) [†]	Moderate	83.37 \pm 11.60	77.75 \pm 6.92	80.25 \pm 6.43
	High	115.10 \pm 7.88	115.90 \pm 13.75	114.10 \pm 8.01
Elimination time (min) ^{*†}	Moderate	263.10 \pm 43.01	246.90 \pm 50.70	232.50 \pm 53.59
	High	422.50 \pm 40.97	404.40 \pm 57.66	370.60 \pm 34.27
Area under BAC curve (mg \cdot 5 min/ml) ^{*†}	Moderate	12.50 \pm 2.49	11.64 \pm 2.50	11.12 \pm 2.57
	High	27.45 \pm 3.98	26.74 \pm 4.43	25.12 \pm 2.46
Disappearance rate (mg/dl/hr) ^{*†}	Moderate	13.66 \pm 1.68	14.35 \pm 1.93	15.57 \pm 2.44
	High	12.88 \pm 1.08	13.44 \pm 2.01	14.83 \pm 1.13

* Midluteal phase different from early follicular phase and ovulation ($p < 0.05$); no difference between early follicular phase and ovulation ($p > 0.05$).

[†] High dose greater than moderate dose ($p < 0.01$).

Table 2. Means and Standard Deviations for Serum Levels of Gonadal and Hypophyseal Hormones across Doses and Menstrual Cycle Phases

Hormones	Dose	Early follicular phase	Ovulation	Midluteal phase
Estradiol (pg/ml)*	Moderate	67.60 ± 14.83	212.40 ± 121.00	167.40 ± 76.89
	High	60.15 ± 17.73	176.80 ± 115.80	198.00 ± 45.31
Progesterone (ng/ml)†	Moderate	2.50 ± 1.52	10.94 ± 10.12	27.05 ± 15.53
	High	3.46 ± 1.94	6.26 ± 4.74	31.77 ± 12.63
Progesterone/estradiol (P ng/ml* 1000/E pg/ml)†	Moderate	41.29 ± 28.94	69.10 ± 68.49	176.60 ± 138.40
	High	61.74 ± 32.34	59.55 ± 63.22	164.90 ± 61.57
Follicle stimulating hormone (MIU/ ml)†	Moderate	7.93 ± 5.03	14.29 ± 11.55	2.38 ± 1.81
	High	6.98 ± 3.60	6.15 ± 3.70	3.66 ± 3.05
Luteinizing hormone (MIU/ml)	Moderate	13.37 ± 13.84	83.92 ± 86.41	5.41 ± 5.10
	High	12.16 ± 9.58	67.03 ± 103.40	11.54 ± 13.9

* Early follicular phase different from ovulation and midluteal phases ($p < 0.01$); no difference between ovulation and midluteal phase ($p > 0.05$).

† Midluteal phase different from early follicular phase and ovulation ($p < 0.01$); no difference between early follicular phase and ovulation ($p > 0.05$).

tradiol ratio, and FSH. Change scores for estradiol levels reflected the difference between the early follicular phase and the average of the other two phases. Table 3 shows the Pearson product-moment correlations and percentages of variance explained between change scores for the alcohol pharmacokinetic measures and the serum hypophyseal and gonadal hormone levels. Although the magnitude of the correlations involving progesterone, progesterone/estradiol ratio, and FSH was substantial (i.e., as high as 0.63), none of the correlation coefficients were statistically significant.

DISCUSSION

Differences in alcohol metabolism were found across phases of the menstrual cycle in moderately drinking women demonstrated to have ovulated during two consecutive cycles in which alcohol was administered on a repeated measures basis. Shorter elimination times, smaller AUCs, and faster disappearance rates characterized the midluteal phase of the menstrual cycle compared with the early follicular and ovulatory phases. Thus, alcohol elimination appeared to be facilitated during the midluteal phase. These findings were consistent for both moderate and high alcohol doses and appear to be robust. They could not be attributed to order effects associated with dose level or the menstrual cycle phase at which women began their experimental sessions. As expected, measures of peak BACs, alcohol elimination, and AUCs showed the significant effects of moderate versus high alcohol dose.

Results do not support contentions that alcohol absorption and peak BACs vary across phases of the menstrual

cycle. Jones and Jones⁵ showed that women absorbed alcohol more rapidly and produced higher peak BACs at the premenstruum, whereas Zeiner and Kegg⁸ found lower peak BACs and slower alcohol elimination associated with the premenstruum. Although acute alcohol intoxication was not studied during the premenstrual phase in this study, there was no indication of higher or lower peak BACs during the early follicular phase of the menstrual cycle when levels of estrogen and progesterone were found to be comparatively low. Similarly, results of the present study are not compatible with accounts suggesting slower alcohol disappearance rates associated with altered levels of estrogens and progesterones resulting from oral contraceptive use.⁷ The limitations of such comparisons are apparent, because groups of oral contraceptive users defined on this generic basis may involve inclusion of women with unsystematically varying levels of estrogens and progesterones. Given the heterogeneity of oral contraceptive medications, it is presumptuous to infer relationships between gonadal hormone levels and alcohol pharmacokinetics without directly measuring hormone levels, particularly if samples sizes are small.

Results showed faster alcohol disappearance, shorter elimination times, and smaller AUCs associated with relatively elevated levels of both estradiol and progesterone characteristic of the midluteal menstrual cycle phase. Marshall et al.¹⁰ did not report similar significant findings, but their data indicated trends in elimination rates and in AUCs which were consistent with present findings. It is possible that the methodological differences between the two studies may account for the lessened effects found by the former research group. For example, Marshall et al.¹⁰ allowed subjects to consume a light breakfast 2 hr prior to

Table 3. Pearson Product-Moment Correlations and Percentages of Variance Explained between Change Scores for Alcohol Pharmacokinetic Variables and Serum Levels of Gonadal and Hypophyseal Hormones

Hormones	n	Elimination time (min)	Area under BAC-time curve (AUC: mg · 5 min/ml)	Disappearance rate (mg/dl/hr)
Estradiol (pg/ml)	8	-0.005 (0.01%)	0.050 (0.25%)	0.240 (5.8%)
Progesterone (ng/ml)	8	-0.412 (17.0%)	-0.326 (10.6%)	0.259 (6.7%)
Progesterone/estradiol (P ng/ml* 1000/E pg/ml)	8	-0.470 (22.1%)	-0.336 (11.3%)	0.261 (6.8%)
Follicle-stimulating hormone (FSH; MIU/ml)	6	0.628 (39.4%)	0.518 (26.9%)	0.139 (1.9%)

alcohol ingestion, and this may have been associated with slower alcohol metabolism. By contrast, subjects in the present study fasted at least 10 hr before testing. Furthermore, BACs in the former study were recorded every 15 min whereas they were recorded every 5 min in the present study. Thus, calculations of AUCs using the trapezoidal method were more accurate in the present study. In any case, the discrepancy between the Marshall et al.¹⁰ study and the present one requires resolution, because these are the only two studies to date reporting data from women known to have ovulated during the cycles under investigation. In other studies this precaution was omitted.

One of the unique features of the present study was measurement of serum levels of progesterone, estradiol, FSH, and LH at the time of each alcohol administration. Radioimmunoassays allowed determination of hormone levels at specific cycle phases and permitted correlational analyses of gonadal and hypophyseal hormones with the indices of alcohol pharmacokinetics. Levels of progesterone and the ratio of progesterone to estradiol increased and FSH levels decreased during the midluteal compared to the early follicular and ovulatory phases. Estradiol levels were elevated during the ovulatory and midluteal phases compared to the early follicular phase, but no differences were observed in LH levels. The increased levels of progesterone and progesterone to estradiol ratio and decreased FSH levels were associated with shorter alcohol elimination times, smaller AUCs, and faster disappearance rates during that phase of the menstrual cycle. Such a pattern suggests a relationship between enhanced alcohol elimination and serum levels of these hormones during the midluteal phase, and the direction and magnitude of the coefficients obtained in correlational analyses tend to support this notion. It is not clear, however, whether progesterone and FSH levels are directly related to enhanced alcohol elimination during the midluteal phase or merely reflect other physiological/endocrinological changes occurring during this phase which, in turn, modulate alcohol metabolism in women.

Many of the studies which have compared responses to acute alcohol intoxication across menstrual cycle phases among moderately drinking women have been criticized for using small samples. Given the demands of this type of investigation, it is not surprising that the sample sizes appear small. This type of study calls for repeated alcohol administrations timed to coincide with discrete phases of ovulatory cycles as defined by RIAs. In their study of nine ovulating women, Marshall et al.¹⁰ took this extra methodological step, but other investigators have assumed ovulation from self-reported BBT readings and menstrual cycle history data. In the present study, the sample size dwindled, because four women were found to have been anovulatory for either one or both menstrual cycles. Problems with collection of blood samples further handicapped sample sizes for the correlational analyses. Since the *F* test for a correlation is primarily a function of sample size,¹⁸

these analyses were limited in terms of statistical power. For example, the correlations of FSH with elimination time and AUC obtained would require sample sizes of 11 and 15, respectively, to reach statistical significance. However, as Marshall et al.¹⁰ argued, a repeated measures study design is robust for detecting intramenstrual variations in alcohol pharmacokinetics, especially for the AUC index.

This was the first study to measure serum levels of estradiol, progesterone, LH, and FSH over two consecutive menstrual cycles on each day of acute alcohol intoxication. The study was also unique in including data only from women who were demonstrated by RIAs of progesterone during the latter part of the cycle to have ovulated. Although findings are in conflict with reports of increased peak BACs and absorption times for any phase of the menstrual cycle, evidence suggests that alcohol elimination varies systematically over menstrual cycle phases among ovulating women. Women eliminated alcohol faster during the midluteal phase of the cycle when progesterone levels and the ratio of progesterone to estrogen levels were elevated and FSH levels were depressed. This association between changes in alcohol metabolism and fluctuating gonadal and hypophyseal hormone levels across menstrual cycle phases does not appear to be mediated by changes in the volume of distribution of alcohol or estimated total body water, and other possible physiological mechanisms require exploration. Although it is tempting to speculate on the implications of these results, findings require replication among similar groups of normally cycling women. In addition, comparisons of alcohol pharmacokinetics during anovulatory and ovulatory cycles within the same subjects are necessary to determine the extent to which fluctuating gonadal and hypophyseal hormone levels account for intraindividual variability in alcohol metabolism.

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