

Citation:

Pepino MY, Steinmeyer AL, Mennella JA. Lactational state modifies alcohol pharmacokinetics in women. *Alcohol clin Exp Res*. 2007; 31 (6): 909-918.

PubMed ID: [17433009](#)

Study Design:

Non-randomized trial with concurrent controls

Class:

C - [Click here](#) for explanation of classification scheme.

Research Design and Implementation Rating:

 **POSITIVE:** See Research Design and Implementation Criteria Checklist below.

Research Purpose:

Considering the physiological adaptations of the digestive system during lactation, the study was to test whether lactation can alter alcohol pharmacokinetics.

Inclusion Criteria:

Healthy, non-smoking women.

Exclusion Criteria:

- Women who were pregnant, lifetime alcohol abstainers or diabetic
- Women whose carbon monoxide (CO) levels, as measured by a CO monitor (Vitalograph Inc., Lenexa, KS), were greater than 10 ppm, or whose body mass index (BMI) was greater than 30kg/m² since smoking and obesity can induce physiological modifications that affect the pharmacokinetic parameters of a variety of drugs, including alcohol.

Description of Study Protocol:**Recruitment**

Subjects were recruited from advertisements in local newspapers, breastfeeding support groups, and the Women, Infants and Children (WIC) Centers throughout the Philadelphia area.

Design

Non-randomized trial with concurrent controls.

Dietary Intake/Dietary Assessment Methodology

Blood alcohol concentration (BAC) levels were used to assess the alcohol levels.

Blinding Used

BAC was an objective assessment.

Intervention

Not applicable.

Statistical Analysis

- Blood alcohol concentration levels and mood states: Analyzed by using separate three-way mixed ANOVA with reproductive state (lactating, formula feeding and nulliparous) as the between-subjects factor and condition (fed and fasted) and time since alcohol post-consumption sampling time as the within-subjects factors
- The classical pharmacokinetic parameters (time-to-peak, peak BAC, β_0 , b_0 , R and AUC): Analyzed with separate mixed ANOVAs with reproductive state as the between-subject factor and condition as the within-subject factor
- Post hoc Fisher least significant difference analyses: Conducted when the ANOVAs revealed significant effects or interactions

- The significance value: $P < 0.05$.

Data Collection Summary:

Timing of Measurements

- Women drank a 0.4g/kg dose of alcohol following a 12-hour overnight fast during one test session (fasted condition) or
- 60 minutes after consuming a standard breakfast during the other test session (fed condition).

Dependent Variables

- Blood alcohol concentration levels: Estimated by having subjects breathe into a fuel-cell sensor analyzer (Alco-Sensor III, St. Louis, MO) at fixed intervals before and after the consumption of the alcoholic beverage: -1, 25, 35, 45, 55, 65, 75, 85, 95, 105, 115, 125, 135, 145, 175 and 205 minutes. BACs from “breath alcohol” measurements was based on the non-invasive nature, simplicity, accuracy and reliability of the method, which has become a standard procedure in alcohol pharmacokinetic studies
- Subjects completed the Addiction Research Center Inventory (ARCI) and the Biphasic Alcohol Effect Scales (BAES) to assess alcohol’s subjective effects before (-30 minutes) and after (25, 55, 85 and 175 minutes) they consumed the alcoholic beverage.

Independent Variables

The alcohol beverage: A 15% v/v solution of 100% alcohol mixed with a non-caloric Strawberry-Kiwi flavored drink (Crystal Lite, Kraft Food Inc., Northfield, IL), aliquoted into two equal volumes and each aliquot was consumed within consecutive five-minute periods.

Control Variables

- Age
- Weight
- Height
- Drinking habits.

Description of Actual Data Sample:

- *Initial N*:
 - Subjects were recruited from advertisements in local newspapers
 - Breastfeeding support groups
 - WIC Centers throughout the Philadelphia area.
- *Attrition (final N)*: Due to exclusion criteria, lack of compliance or procedural difficulties, a total of 44 women were included in analysis
- *Age*: Adult women
- *Ethnicity*: Caucasian, African American, Hispanic, Asian, other ethnic group
- *Other relevant demographics*: Not described
- *Anthropometrics*: Matched for age, weight, height and drinking habits
- *Location*: Philadelphia area, USA.

Summary of Results:

Table 1. Subject Demographics

Women	Lactating	Formula-feeding Women	Nulliparous Women
Number of subjects	20	9	15
Height (m)	1.65±0.01	1.67±0.01	1.66±0.02
Weight (kg)	65.0±1.5	69.0±4.9	67.2±3.2
BMI (kg/m²)	24.1±0.7	24.8±1.8	24.4±0.9
TBW	31.5±0.4	32.8±1.2	32.2±0.9
Parity (number)	1.7±0.1	1.7±0.2	NA
Race/ethnicity (percentage)			

Caucasian	40.0	44.4	40.0
African American	35.0	33.3	26.7
Hispanic	10.0	0.0	6.7
Asian	10.0	0.0	13.3
Other	5.0	22.3	13.3
Alcohol consumption during past three weeks			
Number of standard drinks	4.0±1.5	4.0±1.9	9.5±2.7
Number of drinking occasions	2.5±0.9	1.6±0.6	2.8±0.7

TBW, total body water; BMI, body mass index; NA, not applicable

Table 2. Pharmacokinetic Measures (Mean ± SEM) Obtained From Three Groups of Women (Lactating, Formula Feeding, and Nulliparous) Following the Consumption of a 0.4 g/kg Dose of Alcohol Under Fed and Fasted Conditions and the Average of Both Conditions

Measures	Lactating Women (20)			Formula-feeding Women (9)			Nulliparous Women (15)		
	Fed	Fasted	Both	Fed	Fasted	Both	Fed	Fasted	Both
Time-to-peak BAC (h)^c	0.93±0.07	0.65±0.05	0.79±0.04	0.92±0.10	0.73±0.08	0.83±0.06	0.84±0.08	0.58±0.06	0.71±0.05
Peak BAC(g/L)^{cd}	0.39±0.03	0.69±0.0	0.54±0.03 ^a	0.50±0.04	0.76±0.05	0.63±0.04 ^b	0.46±0.03	0.84±0.04	0.65±0.03
AUC (g/L/h)^{cd}	0.68±0.06	1.30±0.06	0.99±0.05 ^a	0.90±0.09	1.49±0.09	1.20±0.08 ^b	0.86±0.07	1.58±0.07	1.22±0.06 ^b

^a Significantly different than ^b

^c Depicts significant effect of condition

^d Depicts significant effect of group

BAC, blood alcohol concentration; AUC, area under the blood alcohol time curve.

Table 3. Alcohol Elimination Measures (Mean ± SEM) Obtained From Three Groups of Women (Lactating, Formula Feeding, and Nulliparous) Following the Consumption of a 0.4g/kg Dose of Alcohol Under Fed or Fasted Conditions

Measures	Lactating Women		Formula-feeding Women		Nulliparous Women	
	Fed	Fasted	Fed	Fasted	Fed	Fasted
Disappearance rate, β₆₀ (g/L/h)^a	0.18±0.02	0.15±0.02	0.22±0.02	0.17±0.02	0.17±0.01	0.16±0.01
Elimination rate, R (g/kg body weight/h)^a	0.11±0.01	0.09±0.01	0.13±0.01	0.10±0.01	0.10±0.01	0.10±0.01
Total eliminated, b₆₀ (g/h)^a	7.27±0.70	6.58±0.50	9.14±0.79	7.18±0.69	6.90±0.58	6.38±0.50
Number of subjects^b	9/20		7/9		13/15	

Values represent a subset of the women in each of the groups for whom we could calculate these measures.

^a Significant effect of condition

^b Significant effect of group.

Other Findings

- Figures showed BAC time curves in lactating, formula feeding and nulliparous women under the fed and fasted conditions: There were significant main effects of reproductive state on BAC levels [F(2, 41)=4.98; P<0.025], peak BAC [F(2, 41)=4.8; P<0.025], and alcohol AUCs [F(2, 41)=5.3; P<0.01]

- Figures showed alcohol consumption produced both stimulant-like and sedative-like effects, as determined by the ARCI and BAES.

Author Conclusion:

- The systemic availability of alcohol was diminished during lactation
- The reduced availability of alcohol in lactating women did not result in related changes in the subjective effects of alcohol.

Reviewer Comments:

The paper:

- Did not calculate the alcohol elimination measures for most lactating subjects on the day they consumed alcohol after a meal
- Did not determine the effects of lactation on alcohol absorption separately from its effects on alcohol elimination
- Could not discount the possibility that physiological and metabolic adaptations of the digestive system during lactation resulted in different patterns of alcohol elimination.

Research Design and Implementation Criteria Checklist: Primary Research

Relevance Questions

1.	Would implementing the studied intervention or procedure (if found successful) result in improved outcomes for the patients/clients/population group? (Not Applicable for some epidemiological studies)	N/A
2.	Did the authors study an outcome (dependent variable) or topic that the patients/clients/population group would care about?	Yes
3.	Is the focus of the intervention or procedure (independent variable) or topic of study a common issue of concern to nutrition or dietetics practice?	Yes
4.	Is the intervention or procedure feasible? (NA for some epidemiological studies)	Yes

Validity Questions

1.	Was the research question clearly stated?	Yes
1.1.	Was (were) the specific intervention(s) or procedure(s) [independent variable(s)] identified?	Yes
1.2.	Was (were) the outcome(s) [dependent variable(s)] clearly indicated?	Yes
1.3.	Were the target population and setting specified?	Yes
2.	Was the selection of study subjects/patients free from bias?	Yes
2.1.	Were inclusion/exclusion criteria specified (e.g., risk, point in disease progression, diagnostic or prognosis criteria), and with sufficient detail and without omitting criteria critical to the study?	Yes
2.2.	Were criteria applied equally to all study groups?	Yes
2.3.	Were health, demographics, and other characteristics of subjects described?	No
2.4.	Were the subjects/patients a representative sample of the relevant population?	Yes
3.	Were study groups comparable?	Yes
3.1.	Was the method of assigning subjects/patients to groups described and unbiased? (Method of randomization identified if RCT)	Yes
3.2.	Were distribution of disease status, prognostic factors, and other factors (e.g., demographics) similar across study groups at baseline?	???

3.3.	Were concurrent controls used? (Concurrent preferred over historical controls.)	Yes
3.4.	If cohort study or cross-sectional study, were groups comparable on important confounding factors and/or were preexisting differences accounted for by using appropriate adjustments in statistical analysis?	N/A
3.5.	If case control or cross-sectional study, were potential confounding factors comparable for cases and controls? (If case series or trial with subjects serving as own control, this criterion is not applicable. Criterion may not be applicable in some cross-sectional studies.)	N/A
3.6.	If diagnostic test, was there an independent blind comparison with an appropriate reference standard (e.g., "gold standard")?	N/A
4.	Was method of handling withdrawals described?	Yes
4.1.	Were follow-up methods described and the same for all groups?	Yes
4.2.	Was the number, characteristics of withdrawals (i.e., dropouts, lost to follow up, attrition rate) and/or response rate (cross-sectional studies) described for each group? (Follow up goal for a strong study is 80%.)	N/A
4.3.	Were all enrolled subjects/patients (in the original sample) accounted for?	Yes
4.4.	Were reasons for withdrawals similar across groups?	N/A
4.5.	If diagnostic test, was decision to perform reference test not dependent on results of test under study?	N/A
5.	Was blinding used to prevent introduction of bias?	N/A
5.1.	In intervention study, were subjects, clinicians/practitioners, and investigators blinded to treatment group, as appropriate?	N/A
5.2.	Were data collectors blinded for outcomes assessment? (If outcome is measured using an objective test, such as a lab value, this criterion is assumed to be met.)	N/A
5.3.	In cohort study or cross-sectional study, were measurements of outcomes and risk factors blinded?	N/A
5.4.	In case control study, was case definition explicit and case ascertainment not influenced by exposure status?	N/A
5.5.	In diagnostic study, were test results blinded to patient history and other test results?	N/A
6.	Were intervention/therapeutic regimens/exposure factor or procedure and any comparison(s) described in detail? Were intervening factors described?	Yes
6.1.	In RCT or other intervention trial, were protocols described for all regimens studied?	Yes
6.2.	In observational study, were interventions, study settings, and clinicians/provider described?	N/A
6.3.	Was the intensity and duration of the intervention or exposure factor sufficient to produce a meaningful effect?	Yes
6.4.	Was the amount of exposure and, if relevant, subject/patient compliance measured?	Yes
6.5.	Were co-interventions (e.g., ancillary treatments, other therapies) described?	N/A
6.6.	Were extra or unplanned treatments described?	N/A
6.7.	Was the information for 6.4, 6.5, and 6.6 assessed the same way for all groups?	Yes
6.8.	In diagnostic study, were details of test administration and replication sufficient?	N/A
7.	Were outcomes clearly defined and the measurements valid and reliable?	Yes
7.1.	Were primary and secondary endpoints described and relevant to the question?	Yes

7.2.	Were nutrition measures appropriate to question and outcomes of concern?	Yes
7.3.	Was the period of follow-up long enough for important outcome(s) to occur?	Yes
7.4.	Were the observations and measurements based on standard, valid, and reliable data collection instruments/tests/procedures?	No
7.5.	Was the measurement of effect at an appropriate level of precision?	Yes
7.6.	Were other factors accounted for (measured) that could affect outcomes?	Yes
7.7.	Were the measurements conducted consistently across groups?	Yes
8.	Was the statistical analysis appropriate for the study design and type of outcome indicators?	Yes
8.1.	Were statistical analyses adequately described and the results reported appropriately?	Yes
8.2.	Were correct statistical tests used and assumptions of test not violated?	Yes
8.3.	Were statistics reported with levels of significance and/or confidence intervals?	Yes
8.4.	Was "intent to treat" analysis of outcomes done (and as appropriate, was there an analysis of outcomes for those maximally exposed or a dose-response analysis)?	N/A
8.5.	Were adequate adjustments made for effects of confounding factors that might have affected the outcomes (e.g., multivariate analyses)?	Yes
8.6.	Was clinical significance as well as statistical significance reported?	No
8.7.	If negative findings, was a power calculation reported to address type 2 error?	No
9.	Are conclusions supported by results with biases and limitations taken into consideration?	Yes
9.1.	Is there a discussion of findings?	Yes
9.2.	Are biases and study limitations identified and discussed?	Yes
10.	Is bias due to study's funding or sponsorship unlikely?	Yes
10.1.	Were sources of funding and investigators' affiliations described?	Yes
10.2.	Was the study free from apparent conflict of interest?	Yes