Published in final edited form as:

Clin Pharmacol Ther. 2008 December ; 84(6): 710–714. doi:10.1038/clpt.2008.119.

Effects of Breast Pumping on the Pharmacokinetics and Pharmacodynamics of Ethanol During Lactation

MY Pepino¹ and JA Mennella¹

¹Monell Chemical Senses Center, Philadelphia, Pennsylvania, USA.

Abstract

This study tested two hypotheses. First, that breast pumping contributes to the previously observed decrease in ethanol bioavailability in lactating women. second, that the effects of breast pumping are more pronounced when ethanol is consumed after a meal. The within-subject factor was test condition (fed or fasted) and the between-subject factor was experimental group (pumped before, pB; pumped after, pa). Those randomly assigned to the pB group ($N = 8$) breast pumped 1 h before drinking, whereas those assigned to the pa group ($N = 8$) breast pumped 0.6 h after drinking. pumping before drinking significantly decreased blood ethanol concentration ($P < 0.05$) and ethanol bioavailability ($P = 0.05$). pumping after drinking sped up elimination ($P = 0.008$), attenuated ethanol-induced hypothermia ($P = 0.002$), and increased feelings of stimulation ($P = 0.03$). The effects were more pronounced when ethanol was consumed after a meal. Common neural/hormonal responses to food and suckling may contribute additive effects in altering the pharmacokinetics/pharmacodynamics of ethanol, and perhaps of other drugs, during lactation.

Lactating women are therapeutic orphans.¹ Not only are they excluded from the drug development process, but little is known about what the lactating body does with a drug over time (pharmacokinetics) and what the drug does to the body (pharmacodynamics). Recognizing these gaps in knowledge, the US Food and Drug Administration (FDA) released a guidance recommending more clinical research on the effects of the lactational state on drug pharmacokinetics/pharmacodynamics, the extent of drug transfer to milk, and the consequences for both mother and child.¹ Although progress continues to be made in determining how much is transferred at a given point in time,^{2–4} the milk–plasma ratio of a drug does not reflect its pharmacokinetics *over* time. The guidance also highlighted the need to provide a basic framework for the experimental design of clinical lactation studies.¹

In response, some argued that lactation probably exerts insignificant effects and that the emphasis on lactation is misdirected (see Dockets in ref. ¹). However, the few studies in the relevant population, along with the pronounced physiological and metabolic changes that accompany lactation,^{5,6} suggested otherwise. For example, fleroxacin took twice as long to reach peak plasma levels in lactating women, with elimination rates reduced by 25%.^{7,8} Similarly, systemic availability of ethanol, perhaps one of the most commonly used drugs during lactation,⁹ was reduced by 20%,^{10,11} and the consequent mood effects were altered in lactating women when compared with both parous women who formula feed and nulliparous women.¹¹ In this latter study on ethanol pharmacokinetics, the methodologies were identical

© 2008 American Society for Clinical Pharmacology and Therapeutics

Correspondence: JA Mennella (E-mail: mennella@monell.org).

SUPPLEMENTARY MATERIAL is linked to the online version of the paper at <http://www.nature.com/cpt>

CONFLICT OF INTEREST

The authors declared no conflict of interest.

for lactating and nonlactating women, with the exception that the former used a breast pump at the start of the experiment. Pumping ended 1 h before the women drank.

This study builds upon these findings and the body of research showing that neural and endocrine circuitries sustaining lactation are similar to those that control energy balance.¹² Feeding and suckling (by infant or breast pump) elicit similar neural, hormonal, and gut responses that regulate digestive processes in the mother.¹³ Because of these shared circuitries, and because drinking after a meal reduces systemic availability of ethanol,^{14,15} our study tested the hypotheses that breast pumping 1 h before drinking contributes to lactation-related changes in ethanol pharmacokinetics/pharmacodynamics, and that these effects of pumping are more pronounced when ethanol is consumed after a meal.

RESULTS

There were no significant differences between the two groups in pregnancy length (38.3 ± 1.5 and 39.2 ± 0.7 weeks), time since parturition (4.0 ± 0.3 and 4.5 ± 0.3 months), age (33.3 ± 1.0 and 32.3 ± 1.7 years), body mass index (22.0 ± 0.7 and 24.6 ± 1.1 kg/m²), or drinking habits (5.5 ± 2.7 and 4.1 ± 1.0 standard drinks during the past 3 weeks). Nor was there a difference in how women fed their babies. Nine women—five in group PA (pumped after) and four in group PB (pumped before)—were exclusively breastfeeding, and the remaining seven—three in group PA and four in group PB—supplemented breastfeeding with formula or baby foods no more than once a day.

As displayed in Figure 1, blood ethanol concentrations (BECs) significantly changed over time ($P < 0.001$), and the pattern of change was significantly dependent on the timing of breast pumping (main effect of group: $P < 0.05$; hypothesis 1) and on whether the ethanol was consumed before or after a meal (main effect of condition: $P < 0.001$). During the fed condition, BEC levels were significantly lower ($P < 0.001$) and tended to peak later ($P = 0.06$), areas under the curve (AUCs) were smaller ($AUC_{0-0.6\text{ h}}$ and $AUC_{0-3.4\text{ h}}$ P s < 0.001), and ethanol was eliminated faster, as determined by β_{60} , b_{60} , and R (all P s = 0.03; Table 1).

Considering the first hypothesis, women who pumped before drinking (group PB) had lower peak BECs ($P = 0.01$) and reduced systemic availability of ethanol, as evidenced by the smaller $AUC_{0-0.6\text{ h}}$ ($P = 0.05$). Those who did not breast pump until 0.6 h after drinking (group PA) eliminated ethanol faster, as determined by β_{60} ($P = 0.008$), b_{60} ($P = 0.008$), and R ($P = 0.05$). Considering the second hypothesis, most effects of breast pumping were more pronounced in the fed condition (Table 1). To determine how eating a meal and/or breast pumping altered systemic availability of ethanol, we compared each $AUC_{0-0.6\text{ h}}$ with the one obtained when the women drank ethanol after an overnight fast and had not nursed or pumped for the past 2.6 h (group PA, fasted condition). As shown in Table 2, eating a meal before drinking ethanol significantly reduced the systemic availability of ethanol by 38%. If the women also breast pumped within the hour before drinking, availability was reduced even further (58%).

The timing of breast pumping relative to ethanol consumption also affected body temperatures ($P = 0.05$). Ethanol consumption decreased temperatures 1.3–1.9 h later in group PB. Both nadir ($P = 0.002$) and peak ($P = 0.02$) temperatures during fasting were significantly lower in this group. In contrast, pumping near peak BEC prevented this hypothermic effect of ethanol such that temperatures remained steady in the women in group PA (Supplementary Figure S1 online). As shown in Table 1, overall temperatures were lower during fasted than fed conditions in group PB only ($P < 0.01$).

Both groups felt ethanol's sedative effects during the fed ($P = 0.005$) and the fasted ($P < 0.001$) conditions and felt its stimulant effects during the fasted condition ($P = 0.02$). However, the groups differed in how stimulated they felt when ethanol was consumed after a meal ($P = 0.03$).

As Figure 2 illustrates, only group PA felt the stimulant effects of ethanol during the immediate hour after drinking as compared to baseline. The stimulatory effects persisted even after controlling for group differences in BEC ($P < 0.01$). Feelings of sedation were not significantly correlated with feelings of stimulation, which is consistent with the contention that the biphasic effects of ethanol function independently.¹⁶

DISCUSSION

Suckling stimulation, which is critical for sustaining one of the most energy-demanding mammalian activities, altered the way the lactating body handles ethanol and the way ethanol made women feel. The effects of breast pumping depended, in part, on the timing of pumping relative to the consumption of alcohol and on whether ethanol was consumed alone or with a meal. That is, pumping an hour before drinking decreased BEC and reduced its systemic availability, whereas pumping when BEC levels were peaking resulted in faster elimination, with women reporting that they felt the stimulant effects of ethanol. Most effects were more pronounced when ethanol was consumed with a meal.

To put this in perspective, we found that eating a meal before drinking reduced ethanol's systemic availability by 38% and, if lactating women also breast pumped before drinking, systemic availability of ethanol was reduced further to 58%. This suggests that food and breast stimulation have additive effects on ethanol metabolism. It is well known that food increases the metabolism of ethanol during its first passage through the gut and liver before reaching the systemic circulation (i.e., first-pass metabolism^{14,15,17}). It does so directly, by speeding up elimination through enhanced blood flow to the liver and/or activity of ethanol-metabolizing enzymes, or indirectly, by delaying gastric emptying, which decreases the rate of intestinal absorption.^{14,18} Because most ethanol is eliminated through hepatic metabolism via a saturable process, the slower the rate of ethanol delivery from the gut to the liver, the more efficient its first-pass metabolism.¹⁴ We acknowledge that this study could not determine with certainty the effects on ethanol absorption separately from effects on elimination because the ethanol was orally administered. Research is needed that uses breath ethanol concentration clamps to obtain steady-state conditions¹⁸ as well as manipulates the timing and length of breast pumping relative to drinking.

Breastfeeding and breast pumping elicit neural, hormonal, and gut responses similar to those elicited by eating,¹³ but the exact mechanisms underlying their effects on ethanol metabolism remain to be elucidated. Suckling causes prolonged release of hormones (e.g., prolactin and oxytocin) that are necessary for milk production¹⁹ and, similar to what occurs during sham feeding, release of vagally regulated gut hormones (e.g., insulin, gastrin, and cholecystokinin)^{13,20} that modulate mood states and digestive processes in the mother.¹³ The common neural and endocrine circuitries controlling reproduction and energy balance likely evolved, in part, to cope with the high energy demands of lactation¹² because a large flux of nutrients must be mobilized to the mammary tissues for milk synthesis.^{6,21} The findings that ethanol-induced hypothermia²² was attenuated, the stimulatory effects on mood were enhanced, and the elimination of ethanol was faster in those who pumped during peak BEC suggest that pumping has shorter-duration effects on metabolism and mood, perhaps resulting from the aforementioned suckling-induced hormonal changes and activation of brain areas involved in regulating motivation and emotions.

Alcohol, a drug that is regarded as being usually compatible with breastfeeding by many authorities²³ and cultures,²⁴ is unique because of its small molecular weight, amphipathicity, relatively low toxicity, and phase of pseudo zero-order saturation elimination kinetics.²⁵ Whether the lactation-related changes in ethanol pharmacokinetics generalize to other drugs warrants study. Further, if clinical pharmacokinetic studies on lactating women are conducted

in the future, the findings gleaned from this small, basic experimental study suggest the following. First, the timing and duration of breastfeeding or breast pumping should be controlled for in the experimental design. Second, protocols that require both plasma and milk (i.e., pumping required) rather than plasma only may yield different pharmacokinetic data. Third, if postpartum women are used as a control group for pregnant women in clinical pharmacological trials, investigators should describe the lactational status of their subjects and control for the aforementioned variables. As is the case that some medications are taken with a meal for better absorption, this type of research design may reveal the optimum timing relative to breastfeeding for ingesting medication. For example, research could determine whether the timing of breastfeeding in relation to insulin dosing attenuates the erratic insulin patterns and greater variability in glucose control often observed in insulin-dependent diabetic lactating women²⁶ as well as whether the higher between-subject variation in estimated apparent oral clearance, distribution volume, and amount of amoxicillin excreted in postpartum women when compared to pregnant women is due to breastfeeding.²⁷

Recent times witnessed a resurgence in breastfeeding, which is the ideal way to feed and nurture infants.²⁸ Consequently, more women are lactating, many of whom will need and take medication. The present findings provide a potential mechanism underlying the previously observed lactation-related alterations in ethanol pharmacokinetics and pharmacodynamics,¹¹ and an experimental framework upon which future clinical lactation studies of other drugs could be conducted.

METHODS

Participants

Sixteen lactating women at 3–5 months postpartum participated in the study. Exclusion criteria included pregnancy, alcohol dependence or abstinence, diabetes, obesity, and tobacco use. At ~8:30 AM on each day, pregnancy tests were administered, breath carbon monoxide was measured to verify nonsmoking status, and capillary blood glucose levels were measured to ensure that subjects had abstained from eating since the previous night. All procedures were approved by the Office of Regulatory Affairs at the University of Pennsylvania, and each woman gave informed written consent.

Procedures

A within- and between-subject design study was conducted. The within-subject factor was testing condition (fed or fasted), and the between-subject factor was experimental group (PB or PA). Both groups used an electric breast pump (Medela, Crystal Lake, IL) for 16 min (8 min per breast) on two test days separated by 1 week. Subjects randomly assigned to group PB ($N = 8$) breast pumped an hour before drinking, whereas those assigned to group PA ($N = 8$) breast pumped 0.6 h after drinking, having last nursed or breast pumped 2.6 ± 0.7 h prior to ethanol consumption. Because the strength of the applied vacuum from the breast pump can affect lactational performance,²⁹ the same intensity setting on the breast pump, the midway point (-160 mm Hg), was used for all subjects. The infants were not present and therefore no breastfeeding occurred. We did not include a group who refrained from pumping during the entire 4.5-h session because of discomfort and consequences of breast engorgement.

At ~9:00 AM (shortly after group PB finished pumping) and in counterbalanced order, the subjects ingested a standard meal on one test day (fed condition) and continued to fast during the other (fasted condition). This standard meal, which contains 530 calories and was ingested within 10 min, has been used earlier in ethanol pharmacokinetic studies (see refs. ^{11,18}). One hour later (time 0), the subjects drank a 0.4 g/kg dose of ethanol in a palatable, noncaloric, strawberry-kiwi-flavored drink. The alcoholic beverage (15% vol/vol) was aliquoted into two

equal volumes, each consumed within consecutive 5-min periods. BECs estimated from breath (Alco-Sensor IV, St. Louis, MO) and ear temperatures (Braun, Kronberg, Germany) were measured before and at fixed intervals after (beginning at 0.4 and ending at 3.4 h; see Figure 1 and Supplementary Figure S1 online) drinking. Subjects also completed the Biphase Alcohol Effects Scale³⁰ before (−0.5 h) and after (0.4, 0.9, 1.4, and 2.9 h) drinking to determine whether breast pumping altered feelings of stimulation and sedation across the BEC curve.

Classic pharmacokinetic measures

Following established methods,³¹ (we determined peak BEC, time-to-peak BEC, and area under the blood ethanol–time curve (AUC; g·h/l). AUCs were estimated using a software program (OriginLab, Northampton, MA) based on the trapezoidal rule. Two AUCs were calculated for each condition. One focused on the entire session (AUC_{0–3.4 h}), and the other on the time from ethanol ingestion (time 0) until 0.6 h (AUC_{0–0.6 h}), the time after which group PA began pumping. Thus, any group differences in AUC_{0–0.6 h} would be due to the fact that one group breast pumped before ethanol ingestion whereas the other did not.

Linear least-squares regression lines were calculated within the apparent linear portion of the descending limb of the BEC time curve for each subject and each condition.³¹ The slopes of these regression lines represent the ethanol disappearance rate (β_{60} ; g/l/h). To exclude the upper distribution phase and lower first-order elimination phase of the linear portion of the curve, we used the first value taken 0.5 h after peak BEC and all subsequent readings ≥ 0.20 g/l. β_{60} could not be calculated for two of the women in the fed condition because there were not enough BEC values ≥ 0.20 g/l. The correlation coefficients for these regression lines ranged from −0.97 to −0.89 (mean + SD = −0.97 + 0.03) for the fasted condition and −1.00 to −0.91 (mean + SD = −0.96 ± 0.03) for the fed condition. The total amount of ethanol eliminated from the body per hour, b_{60} , was calculated as $b_{60} = \beta_{60} \times \text{TBW}/B_w$, where TBW (total body water) was calculated as $\text{TBW} = (0.1069 \times \text{height (cm)}) + (0.2466 \times \text{weight (kg)}) - 2.097$ and $B_w = 0.80$. This standardized anthropometric equation estimates TBW in women with a precision of ± 9 – 11% .^{31–33}

Data analyses

Dependent variables included BEC levels, classic pharmacokinetic parameters, ear temperatures, and feelings of stimulation and sedation. Separate mixed analyses of variance were carried out for each dependent variable, with group (PB or PA) as the between-subject factor, and condition (fed or fasting) and time since ethanol consumption (where applicable) as within-subject factors. Peak BEC was a covariate for Biphase Alcohol Effects Scale analyses to ensure that any group differences were not due to BEC differences. When analyses of variance revealed significant effects, *post hoc* Fisher least significant difference analyses were conducted. If the sphericity assumption of the analysis of variance was violated, Geisser corrections were used. All analyses were performed using STATISTICA (StatSoft, Tulsa, OK), and the criterion for statistical significance was $P \leq 0.05$.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

ACKNOWLEDGMENTS

This study was supported by National Institutes of Health grant AA09523. We gratefully acknowledge the skillful technical assistance of Allison Steinmeyer and Emily Perlman. We also thank Kristin L. Field, Gary K. Beauchamp, Leslie Stein, and Catherine Forestell for their valuable comments on the manuscript.

References

- Food and Drug Administration. Guidance for industry on clinical lactation studies: Study design, data analysis, and recommendations for labeling.. Draft guidance. [28 April 2008]. 2 February 2005 <<http://www.fda.gov/ohrms/dockets/DOCKETS/05d0030/05d0030.htm>>
- Hale, TW. Medications and Mother's Milk. Vol. 12th edn. Hale Publishing; Amarillo, TX: 2006.
- United States National Library of Medicine. TOXNET. [28 April 2008]. Last modified 10 September 2007. <<http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?LACT>>
- Ito S. Drug therapy for breast-feeding women. *N. Engl. J. Med* 2000;343:118–126. [PubMed: 10891521]
- Dufour DL, Sauter ML. Comparative and evolutionary dimensions of the energetics of human pregnancy and lactation. *Am. J. Hum. Biol* 2002;14:584–602. [PubMed: 12203813]
- Prentice AM, Prentice A. Energy costs of lactation. *Annu. Rev. Nutr* 1988;8:63–79. [PubMed: 3060180]
- Dan M, Weidekamm E, Sagiv R, Portmann R, Zakut H. Penetration of feroxacin into breast milk and pharmacokinetics in lactating women. *Antimicrob. Agents Chemother* 1993;37:293–296. [PubMed: 8452360]
- Weidekamm E, Portmann R, Suter K, Partos C, Dell D, Lucker PW. Single- and multiple-dose pharmacokinetics of feroxacin, a trifluorinated quinolone, in humans. *Antimicrob. Agents Chemother* 1987;31:1909–1914. [PubMed: 3125788]
- Little RE, Anderson KW, Ervin CH, Worthington-Roberts B, Clarren SK. Maternal alcohol use during breast-feeding and infant mental and motor development at one year. *N. Engl. J. Med* 1989;321:425–430. [PubMed: 2761576]
- da-Silva VA, Malheiros LR, Moraes-Santos AR, Barzano MA, McLean AE. Ethanol pharmacokinetics in lactating women. *Braz. J. Med. Biol. Res* 1993;26:1097–1103. [PubMed: 8312842]
- Pepino MY, Steinmeyer AL, Mennella JA. Lactational state modifies alcohol pharmacokinetics in women. *Alcohol. Clin. Exp. Res* 2007;31:909–918. [PubMed: 17433009]
- Wade GN, Schneider JE. Metabolic fuels and reproduction in female mammals. *Neurosci. Biobehav. Rev* 1992;16:235–272. [PubMed: 1630733]
- Uvnas-Moberg K, Widstrom AM, Marchini G, Winberg J. Release of GI hormones in mother and infant by sensory stimulation. *Acta Paediatr. Scand* 1987;76:851–860. [PubMed: 3321889]
- Levitt DG. PKQuest: measurement of intestinal absorption and first pass metabolism - application to human ethanol pharmacokinetics. *B.M.C. Clin. Pharmacol* 2002;2:4.
- Gentry RT. Effect of food on the pharmacokinetics of alcohol absorption. *Alcohol. Clin. Exp. Res* 2000;24:403–404. [PubMed: 10798565]
- Holdstock L, de Wit H. Individual differences in the biphasic effects of ethanol. *Alcohol. Clin. Exp. Res* 1998;22:1903–1111. [PubMed: 9884132]
- Hahn RG, Norberg A, Gabrielsson J, Danielsson A, Jones AW. Eating a meal increases the clearance of ethanol given by intravenous infusion. *Alcohol Alcohol* 1994;29:673–677. [PubMed: 7695782]
- Ramchandani VA, Kwo PY, Li TK. Effect of food and food composition on alcohol elimination rates in healthy men and women. *J. Clin. Pharmacol* 2001;41:1345–1350. [PubMed: 11762562]
- Mennella JA, Pepino MY, Teff KL. Acute alcohol consumption disrupts the hormonal milieu of lactating women. *J. Clin. Endocrinol. Metab* 2005;90:1979–1985. [PubMed: 15623810]
- Holst N, Jenssen TG, Burhol PG, Jorde R, Maltau JM, Haug E. Gut peptides in lactation. *Br. J. Obstet. Gynaecol* 1986;93:188–193. [PubMed: 2868752]
- Dewey KG. Energy and protein requirements during lactation. *Annu. Rev. Nutr* 1997;17:19–36. [PubMed: 9240917]
- Danel T, Libersa C, Touitou Y. The effect of alcohol consumption on the circadian control of human core body temperature is time dependent. *Am. J. Physiol. Regul. Integr. Comp. Physiol* 2001;281:R52–R55. [PubMed: 11404278]
- American Academy of Pediatrics: Committee on Drugs. Transfer of drugs and other chemicals into human milk. *Pediatrics* 2001;108:776–789. [PubMed: 11533352]

24. Mennella, JA. Alcohol use during lactation: Effects on the mother and breastfeeding infant.. In: Watson, RR., editor. Nutrition and Alcohol. Vol. 2nd edn.. CRC Press; Boca Raton, FL: 2004. p. 377-391.
25. Lee SL, Chau GY, Yao CT, Wu CW, Yin SJ. Functional assessment of human alcohol dehydrogenase family in ethanol metabolism: significance of first-pass metabolism. *Alcohol Clin. Exp. Res* 2006;30:1132–1142. [PubMed: 16792560]
26. Murtaugh MA, Ferris AM, Capacchione CM, Reece EA. Energy intake and glycemia in lactating women with type 1 diabetes. *J. Am. Diet. Assoc* 1998;98:642–648. [PubMed: 9627620]
27. Andrew MA, et al. Amoxicillin pharmacokinetics in pregnant women: modeling and simulations of dosage strategies. *Clin. Pharmacol. Ther* 2007;81:547–556. [PubMed: 17329990]
28. Ryan AS, Wenjun Z, Acosta A. Breastfeeding continues to increase into the new millennium. *Pediatrics* 2002;110:1103–1109. [PubMed: 12456906]
29. Kent JC, et al. Importance of vacuum for breastmilk expression. *Breastfeed. Med* 2008;3:11–19. [PubMed: 18333764]
30. Martin CS, Earleywine M, Musty RE, Perrine MW, Swift RM. Development and validation of the Biphasic Alcohol Effects Scale. *Alcohol. Clin. Exp. Res* 1993;17:140–146. [PubMed: 8452195]
31. Mumenthaler MS, Taylor JL, O'Hara R, Fisch HU, Yesavage JA. Effects of menstrual cycle and female sex steroids on ethanol pharmacokinetics. *Alcohol. Clin. Exp. Res* 1999;23:250–255. [PubMed: 10069553]
32. Watson PE, Watson ID, Batt RD. Total body water volumes for adult males and females estimated from simple anthropometric measurements. *Am. J. Clin. Nutr* 1980;33:27–39. [PubMed: 6986753]
33. Brick J. Standardization of alcohol calculations in research. *Alcohol. Clin. Exp. Res* 2006;30:1276–1287. [PubMed: 16899030]

Figure 1.

Blood ethanol concentration curves over time in the two groups of lactating women. Group PB ($N = 8$; circles) breast pumped 1 h before, whereas group PA ($N = 8$; triangles) breast pumped beginning 0.6 h after drinking a 0.4 g dose of ethanol per kg of body weight. Open symbols depict values obtained during the overnight fasted condition, and closed symbols depict values obtained during the fed condition. The timing of breast pumping is indicated by the hatched box, and meal ingestion (for the fed condition) is shown by an arrow. There was a significant interaction between group and time [$F(14,196) = 3.65$; $P < 0.05$] and the effect of condition (fed or fasting) was also significant [$F(14,196) = 11.38$; $P < 0.001$].

Figure 2.

Feelings of stimulation, as measured by the Biphasic Alcohol Effects Scale (BAES), during the fed condition. Group PA ($N = 8$; circles) breast pumped 1 h before, whereas Group PB ($N = 8$; triangles) breast pumped beginning 0.6 h after drinking ethanol, when blood ethanol concentrations were near peak levels. Group PB felt more of the stimulant effects of ethanol.

* $P < 0.05$ when compared to respective baseline values. PA, pumped after; PB, pumped before.

Table 1

Effects of timing of breast pumping stimulation relative to ethanol consumption and fed/fasted condition on ethanol pharmacokinetics and ear temperatures^a

	Fed condition		Fasted condition		Combined fed and fasted	
	Group PB	Group PA	Group PB	Group PA	Group PB	Group PA
Pharmacokinetic outcomes						
Peak BEC (g/l)	0.36 ± 0.03^{b,c}	0.46 ± 0.03^c	0.67 ± 0.03	0.72 ± 0.03	0.51 ± 0.02^b	0.59 ± 0.02
Time-to-peak BEC (h)	0.98 ± 0.10^c	0.81 ± 0.10	0.67 ± 0.09	0.71 ± 0.09	0.82 ± 0.06	0.76 ± 0.06
Disappearance rate, β_{00} (g/l/h) ^d	0.15 ± 0.02^b	0.21 ± 0.02^c	0.13 ± 0.01^b	0.17 ± 0.01	0.14 ± 0.01^b	0.19 ± 0.01
Elimination rate, R (g/kg/h) ^d	0.10 ± 0.01	0.13 ± 0.01^c	0.08 ± 0.01^b	0.10 ± 0.01	0.09 ± 0.01^b	0.12 ± 0.01
Total eliminated, b_{00} (g/h) ^d	5.81 ± 0.71^b	8.34 ± 0.61^c	4.98 ± 0.43^b	6.84 ± 0.37	5.39 ± 0.46^b	7.59 ± 0.40
AUC (0-3.4 h) (g·h/l)	0.68 ± 0.07^c	0.83 ± 0.07^c	1.25 ± 0.07	1.37 ± 0.07	0.97 ± 0.06	1.10 ± 0.06
AUC (0-6 h) (g·h/l)	0.10 ± 0.02^{b,c}	0.15 ± 0.02^c	0.22 ± 0.02	0.24 ± 0.02	0.16 ± 0.01^b	0.19 ± 0.01
Temperature outcomes						
Mean temperature (°C) ^e	35.6 ± 0.6^c	35.8 ± 0.6	35.0 ± 0.6^b	35.6 ± 0.6	35.3 ± 0.2	35.7 ± 0.2
Peak temperature (°C) ^e	36.1 ± 0.1^c	36.1 ± 0.2	35.4 ± 0.1^b	35.9 ± 0.1	35.8 ± 0.1	36.0 ± 0.1
Time-to-peak (h) ^e	1.1 ± 0.4	1.5 ± 0.4	1.9 ± 0.5	1.5 ± 0.4	1.5 ± 0.2	1.5 ± 0.2
Nadir temperature (°C) ^e	35.0 ± 0.2^c	35.4 ± 0.2	34.5 ± 0.2^b	35.3 ± 0.2	34.7 ± 0.2^b	35.4 ± 0.2
Time-to-nadir (h) ^e	2.1 ± 0.4	1.8 ± 0.3	1.3 ± 0.3	1.3 ± 0.3	1.7 ± 0.2	1.5 ± 0.2

AUC, area under the curve; BEC, blood ethanol concentration; PA, pumped after; PB, pumped before.

^aValues represent mean ± SEM of eight women in group PB and eight women in group PA, unless otherwise indicated. Significant effects are indicated by boldface.

^b $p \leq 0.05$ for the comparison with same condition, group PA.

^c $p \leq 0.05$ for the comparison with fasted condition, same group.

^dValues represent data from six women in group PB and eight women in group PA (see text for details).

^eValues represent data from seven women in group PB and eight women in group PA.

Table 2

Relative effects of breast pump stimulation and drinking during fed or fasted conditions on the systemic availability of ethanol during the first 0.6 h after consumption ($AUC_{0-0.6\text{ h}}$)^a

	Group PA	Group PB
Fasted condition	0.24 ± 0.02	0.22 ± 0.02
	—	↓ 8.3%
Fed condition	0.15 ± 0.02^{b,c}	0.10 ± 0.02^{b,c,d}
	↓ 37.5%	↓ 58.3%

AUC, area under the curve; PA, pumped after; PB, pumped before.

^a AUC values during first 0.6 h after ethanol consumption are expressed as g·h/l. Values are mean ± SEM. The relative percentages were obtained by calculating the difference between each $AUC_{0-0.6\text{ h}}$ and the $AUC_{0-0.6\text{ h}}$ obtained from group PA in the fasted condition, divided by the $AUC_{0-0.6\text{ h}}$ of group PA in the fasted condition, and then multiplied by 100. Significant effects are indicated by boldface.

^b $P < 0.001$ for the comparison with $AUC_{0-0.6\text{ h}}$ obtained in the fasted condition, group PA.

^c $P < 0.001$ for the comparison with $AUC_{0-0.6\text{ h}}$ obtained in the fasted condition, same group.

^d $P < 0.05$ for the comparison with $AUC_{0-0.6\text{ h}}$ obtained in the fed condition, group PA.