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Acute Effect of Alcohol on Estradiol, Estrone, Progesterone, Prolactin, Cortisol, and Luteinizing Hormone in Premenopausal Women

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Background: Heavy alcohol consumption is associated with menstrual irregularities, including anovulation, luteal-phase dysfunction, recurrent amenorrhea, and early menopause. In addition, moderate to heavy alcohol intake has been found to increase the risk of spontaneous abortions and breast cancer. These adverse effects could at least in part originate from alcohol-mediated changes in hormone levels.

Methods: The acute effect of alcohol on the hormone balance in women using oral contraceptives (OC+) and also in nonusers (OC−), was evaluated in 30 OC− and 31 OC+ subjects, representing the whole period of the menstrual cycle. It was also evaluated in 40 OC− and 47 OC+ subjects during the midcycle phase and in 10 OC+ subjects with unknown cycle phase.

Results: We found that among subjects who used oral contraceptives, estradiol levels increased and progesterone levels decreased after intake of alcohol (0.5 g/kg). No dose effect (0.34–1.02 g/kg) on progesterone was observed in a substudy on 10 OC+ subjects. With regard to estrone levels, no effect was observed, although a significant increase was found in the estradiol-to-estrone ratio. Among subjects not using oral contraceptives, progesterone levels decreased after intake of alcohol (0.5 g/kg). No effect was found in estradiol, estrone, or the estradiol-to-estrone ratio during midcycle in this study group. A transient elevating effect of alcohol (0.5 g/kg) on prolactin levels was observed in both study groups. We found that alcohol (0.5 g/kg) had no significant effect on luteinizing hormone (LH) levels among subjects not using oral contraceptives, and observed a decline among subjects using oral contraceptives at midcycle.

Conclusions: We suggest that the estradiol and progesterone effects are related to decreased steroid catabolism, resulting from the alcohol-mediated increase in the hepatic NADH-to-NAD ratio. The transient effect on prolactin levels may reflect acute changes in opioid and dopamine levels in the hypothalamus. The present findings regarding female sex steroids may be of relevance in the association between moderate to heavy alcohol consumption and the development of breast cancer.

Key Words: Premenopausal Women, Oral Contraceptive, Hormone, Acute Effect of Alcohol.

H EAVY ALCOHOL CONSUMPTION is associated with menstrual irregularities, including anovulation, luteal-phase dysfunction, recurrent amenorrhea, and early menopause (Hugues et al., 1980). In addition, moderate to heavy alcohol intake has been found to increase the risk of spontaneous abortions (Harlap and Shiono, 1980; Kline et al., 1980) and breast cancer (Smith-Warner et al., 1998). It seems reasonable to hypothesize that these adverse effects could at least in part originate from alcohol-mediated changes in hormone levels.

Several studies have focused on the acute effect of alcohol on the hormonal balance in women. No effects on LH or FSH have been demonstrated (McNamee et al., 1979; Mendelson et al., 1981, 1987; Välimäki et al., 1983; Teoh et al., 1988; Becker et al., 1988; Mendelson et al., 1989). However, prolactin reportedly rises in the beginning of intoxication (Mendelson et al., 1987), with a subsequent decline at 2–4 hr from the start of drinking (Välimäki et al., 1983). Reports also indicate that acute alcohol intake elevates estradiol levels among both premenopausal women (Välimäki et al., 1983; Mendelson et al., 1987, 1989; Teoh et al., 1988; Teoh et al., 1990; Mendelson et al., 1988) and postmenopausal women on estrogen replacement therapy (Ginsburg et al., 1996). To our knowledge, no data have been published on the acute effect on estrone levels among premenopausal women, although an acute decline in estrone levels among postmenopausal women on estrogen replacement therapy has been described (Ginsburg et al., 1996). Several studies have found no effect of alcohol on progesterone during nonstimulated basal conditions (McNamee et al., 1979; Välimäki et al., 1983; Mendelson et al., 1987, 1989; Teoh et al., 1988). Although cortisol has been

extensively studied in males, there have been only a few studies in females, and those indicate a semiacute elevating effect that occurs only at higher alcohol doses at 8 hr from start of drinking (Ekman et al., 1994). Lowered cortisol levels in response to alcohol intake has been described among sons of alcoholics (Schuckit et al., 1987).

Most of the studies mentioned have included less than 10 subjects, and as a consequence, only the more prominent acute effects have been detected because of a lack of statistical power. None of the studies have included women taking oral contraceptives, the use of which is highly prevalent among women during the reproductive years of their lives. This report includes data from three substudies on the acute effect of alcohol on progesterone, estradiol, estrone, cortisol, LH, and prolactin among healthy premenopausal women using oral contraceptives, as well as among nonusers.

METHODS

Study Subjects

Healthy nonpregnant Caucasian female volunteers were recruited by advertising in a local newspaper and on a poster board at the dormitory of a local medical student association and at the University of Helsinki. The studies were conducted in accordance with the guidelines proposed in The Declaration of Helsinki and were approved by a local ethical committee. A questionnaire was sent to all subjects, and participation was confirmed by obtaining a signed informed consent, together with the filled-in questionnaire. In addition, subjects were interviewed by phone to exclude those with alcohol abuse. All subjects included had a history of regular menses, and none used any medication other than oral contraceptives containing ethinyl estradiol (mean 29 μg, range 20–40 μg) and a progestin. All the oral contraceptive subjects, but none of the subjects in the nonoral contraceptive group, reported regular use of oral contraceptives for several months before entering the study. None of the study subjects had a record of hirsutism or other disease.

In substudy A, the OC+ group consisted of 31 subjects [age 24 ± 3 yr (range 20–31) and body weight 59 ± 4 kg (range 50–65)] and the OC− group of 30 subjects [age 24 ± 4 yr (range 19–33) and body weight 62 ± 6 kg (range 53–80)]. Participation in the sessions was random with respect to menstrual cycle phase.

In substudy B, the OC+ group consisted of 47 subjects [age 26 ± 4 yr (range 19–38), body mass index 21.2 ± 2.1 kg/m² (range 16.8–26.4)], and the OC− group consisted of 40 subjects [age 30 ± 7 yr (range 19–46), body mass index 21.5 ± 2.2 kg/m² (range 17.0–27.4)]. Four OC+ subjects with high estradiol and estrone levels (685 and 1267 pmol/l; 304 and 254 pmol/l; 248 and 148 pmol/l; 141 and 65 pmol/l), indicating significant ovarial activity despite regular use of oral contraceptives, were excluded from analysis. Participation in the sessions was scheduled as close as possible to the midcycle phase with reference to the phase reported in the questionnaire [cycle day 18 ± 3 (range 7–26) for OC+ subjects and cycle day 15 ± 4 (range 8–21) for OC− subjects].

Substudy C included 10 subjects using oral contraceptives [age 20–32 yr (mean 24 yr) and weight 52–63 kg (mean 58 kg)]. The menstrual cycle phase was not recorded.

Study Procedures

All subjects participated randomly in one placebo- and one alcohol- (0.5 g/kg diluted in 10% w/v lingonberry juice) drinking event. The intervening time was 28 days, except for substudy C, which consisted of one placebo- and three alcohol- (0.34 g/kg, 0.68 g/kg, and 1.02 g/kg diluted in 10% w/v) drinking events in random order, with intervals of 1 week or

more in between. The placebo drink contained an equal volume of lingonberry juice. All drinking events started at 6 PM. All subjects were told not to drink any alcohol on the previous evening. No instructions were given regarding meals and snacks. The subjects were seated throughout the experiment. The drinking time was 30 min. Blood samples were taken from the median cubital vein before and at different time points (60 and 120 min for substudy A; 45 and 90 min for substudy B; 40, 90, and 150 min for substudy C) after the start of drinking. Ethanol levels increased to 8.4 ± 0.3 mM (0.39 ± 0.01 g/l at 60 min) and to 7.1 ± 0.3 mM (0.33 ± 0.01 g/l at 90 min) in substudies A and B, respectively (dose 0.5 g/kg). In substudy C, ethanol levels increased to 5.2 ± 0.6 mM (0.24 ± 0.03 g/l at 90 min) with the dose of 0.34 g/kg; to 13.2 ± 1.0 mM (0.61 ± 0.05 g/l at 150 min) with the dose of 0.68 g/kg; and to 25.6 ± 0.6 mM (1.17 ± 0.03 g/l at 150 min) with the dose of 1.02 g/kg.

Analytical Procedures

Blood samples were collected in tubes containing 22.5 mg of sodium fluoride and 22.5 mg of potassium oxalate as anticoagulants for a volume of 10 ml blood. Plasma samples were prepared within 4 hr and stored at −70°C until determinations. Ethanol levels were determined from plasma by headspace gas chromatography (Perkin-Elmer F40). Estrone levels [within-assay variability 13.2% at the level of 32 pmol/l ($n = 14$) and between-assay variability 6.8% at the level of 133 pmol/l ($n = 7$)], progesterone levels [within-assay variability 7.9% at the level of 1.56 nmol/l and between-assay variability 8.1% at the level of 1.62 nmol/l ($n = 10$)], cortisol levels [within-assay variability 2.1% at the level of 146 nmol/l and between-assay variability 5.2% at the level of 31.2 nmol/l ($n = 10$)], LH levels [within-assay variability 2.9% at the level of 5.6 U/l and between-assay variability 11.0% at the level of 4.11 U/l ($n = 10$)], and prolactin levels (within-assay variability 9.5% at the level of 8 μg/l) were determined by standard radioimmunoassay reagent sets [Diagnostic System Laboratories (DSL-8700), USA, for estrone; Orion Diagnostica, Finland, for progesterone and cortisol; Farmos Diagnostica, Finland, for LH; Kabi Pharmacia Diagnostics, Sweden, for prolactin]. Estradiol levels [within-assay variability 9.7% at the level of 103 pmol/l and between-assay variability 5.1% at the level 394 pmol/l ($n = 10$)] were determined for OC− subjects by a standard radioimmunoassay reagent set from Orion Diagnostica, Finland. To increase the sensitivity of the estradiol determinations for OC+ subjects in substudy B, a standard radioimmunoassay reagent set from Diagnostic System Laboratories (DSL-39100), USA, was used [within-assay variability 14% at the level of 17 pmol/l and between-assay variability 22% at the level 30 pmol/l ($n = 5$), detection limit 2.2 pmol/l]. All determinations were made in duplicate.

Data Analyses

The results are expressed as mean ± SEM if not otherwise specified. The baseline hormone level is defined as the mean of levels before the start of drinking at alcohol- and placebo-drinking sessions 4 weeks apart. The effect of alcohol on hormone levels is defined as the individual change in concentration (%) observed during the placebo session subtracted from the individual change in concentration observed during the alcohol-drinking session. Power calculations for matched-sample t's were made as described (Howell, 1992). With type I error (α) set at 5% and a test power (1-β) of 80%, it was estimated that the detectable change in hormone levels should be in the range of 13–24% for both OC− and OC+ subjects in the separate substudies. Statistical significance in the separate substudies was tested by analysis of variance for repeated measures (drug and time as within-group factors), followed by matched paired t-test. In the overall analysis with substudies A and B combined (OC− and OC+ subjects analyzed separately), the substudy was included in the analysis of variance as a between-group factor. In the analysis of variance, the absolute hormone values were used if not otherwise specified. The reported F values represent the drug by time interaction. The Student's t-test or the Mann Whitney U test was used when comparing baseline hormone levels of OC− and OC+ subjects in the same substudy. Data were analyzed by using SPSS (version 6.1) and GraphPad Prism (version 2.0) statistical software.

Table 1. Baseline Hormone Levels in the Study Populations (Mean ± SD)

	Oral contraceptive (−)		Oral contraceptive (+)		
	Substudy A (n = 30)	Substudy B (n = 40)	Substudy A (n = 31)	Substudy B (n = 47)	Substudy C (n = 10)
Estradiol (pmol/l)	80 ± 37[a] 291 ± 140[b]	245 ± 157	ND	36 ± 12***	ND
Estrone (pmol/l)	ND	152 ± 80	ND	30 ± 20***	ND
Progesterone (nmol/l)	1.6 ± 0.9[c] 27.9 ± 15.5[d]	8.7 ± 10.5	1.1 ± 0.4***	0.7 ± 0.4***	1.1 ± 0.3
Prolactin (μg/l)	6.6 ± 3.8	10.4 ± 4.5	6.5 ± 2.7	13.3 ± 6.7*	ND
Cortisol (nmol/l)	223 ± 140	225 ± 93	325 ± 110***	350 ± 135***	317 ± 74
LH (IU/l)	5.4 ± 4.2	ND	2.7 ± 2.1***	ND	ND

Reported cycle days [a] 1–11 (n = 14); [b] 12–28 (n = 16); [c] 1–15 (n = 19); [d] 16–28 (n = 11); ND = not determined.
* p < 0.05 and *** p < 0.001 compared with subjects in the same substudy not using oral contraceptives.

Table 2. Effect of Alcohol (Mean and 95% Confidence Intervals) on Hormone Levels Among Women Using Oral Contraceptives (OC+)

	Time from intake in							
	Substudy A				Substudy B			
	60 min		120 min		45 min		90 min	
	Mean	95% CI	Mean	95% CI	Mean	95% CI	Mean	95% CI
Estradiol	ND		ND		+29%	(+16,+41)***	+25%	(+9,+41)***
Estrone	ND		ND		−3%	(−21,+15)	−8%	(−27,+11)
Progesterone	−12%	(−21,−3)*	−6%	(−15,+3)	−17%	(−27,−8)**	−17%	(−25,−10)***
Prolactin	+19%	(+7,+32)**	−8%	(−17,+1)	+9%	(−9,+26)	+2%	(−18,+22)
Cortisol	−5%	(−12,+2)	−1%	(−10,+7)	+1%	(−7,+9)	+0.2%	(−10,+11)
LH	+1%	(−12,+14)	−15%	(−33,+4)	ND		ND	

ND = not determined.
* p < 0.05, ** p < 0.01, *** p < 0.001 changes during alcohol and placebo conditions compared.

RESULTS

Estradiol and Estrone Levels

The baseline estradiol and estrone levels were clearly suppressed among subjects using oral contraceptives (Table 1). A significant alcohol-mediated elevation in estradiol levels relative to placebo was observed among OC+ subjects ($F = 4.9, p = 0.012$, Table 2). No effect of alcohol was observed in estrone levels, but the estradiol-to-estrone ratio was significantly elevated relative to placebo ($F = 6.9, p = 0.018$). No significant effect of alcohol on estradiol, estrone, or the estradiol-to-estrone ratio was observed among OC− subjects during midcycle in substudy B (Table 3 and Fig. 1). In a subanalysis of OC− subjects (excluding days 9–17 of the menstrual cycle), a tendency for a decline in estradiol levels relative to placebo was observed in substudy A ($F = 3.1, p = 0.07, n = 14$).

Progesterone Levels

The baseline progesterone level was clearly suppressed among subjects using oral contraceptives (Table 1). An alcohol-mediated decline in progesterone levels was observed among both OC+ and OC− subjects. A significant effect of alcohol on progesterone levels was observed in substudy A ($F = 3.4, p = 0.04$) and tendencies in substudies B and C ($F = 1.79, p = 0.17$ and $F = 1.8, p = 0.076$) among OC+ subjects. However, with relative values, the effects were significant in all substudies with lower progesterone levels relative to placebo ($F = 4.3, p = 0.049$ for substudy A; $F = 4.1, p = 0.050$ for substudy B; $F = 6.7, p = 0.002$ for
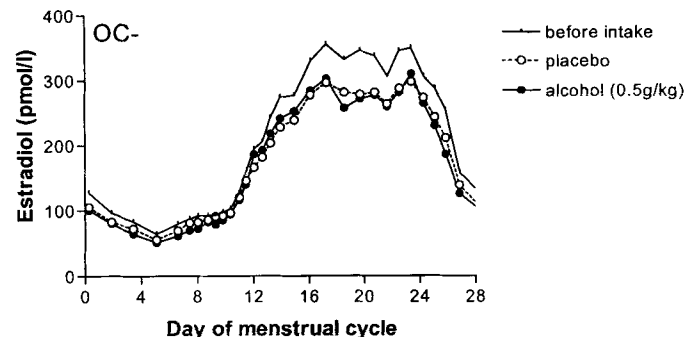

Fig. 1. Estradiol levels before and after intake of placebo or alcohol among 30 subjects not using oral contraceptives (OC−, substudy A). The level before intake represents the mean of the alcohol and placebo session. Placebo and alcohol marks represent the mean of the average changes seen at 60 and 120 min from the start of drinking. The figure is arranged so that a mark shares four data points with marks adjacent to it, with three marks one position away, with two marks two positions away, and so on, and none with five marks or more positions away from it, thus making it the mean of a running frame of five observations. The overall difference between alcohol and placebo is not statistically significant.

substudy C) (Table 2; Figs. 2 and 3). No effect of dose was observed (Fig. 3). Among OC− subjects, a decline in progesterone levels was observed in substudy A ($F = 10.1, p = 0.004$) and a tendency for a decline in substudy B ($F = 1.9, p = 0.16$) (Table 3). In the overall analysis with substudies A and B combined, the effect was significant ($F = 5.7, p = 0.004$) among OC− subjects.

Prolactin, Luteinizing Hormone, and Cortisol Levels

The baseline prolactin levels were correlated with the day of menstrual cycle among OC+ subjects ($r = 0.43, p =$
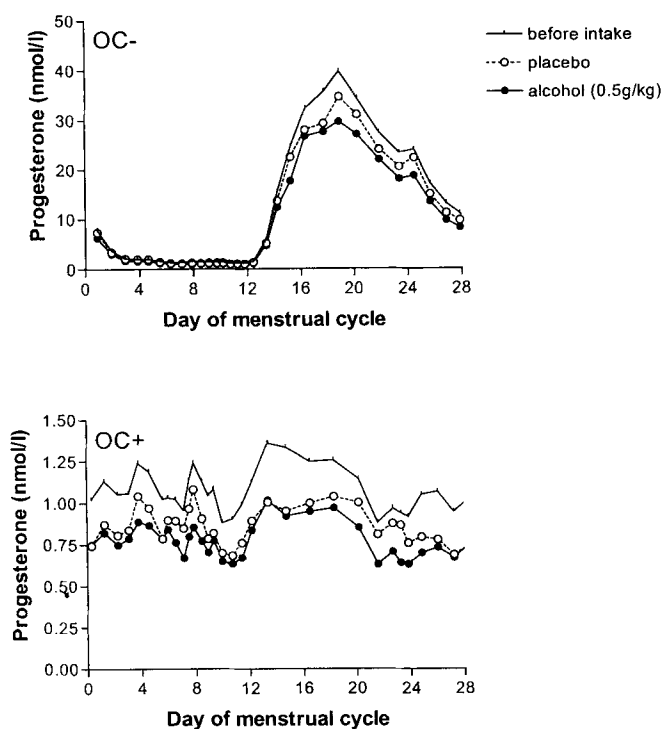
Fig. 2. Progesterone levels before and after intake of placebo or alcohol among 31 subjects using oral contraceptives (OC+, substudy A) and 30 subjects not using oral contraceptives (OC−). See legend to Fig. 1 for explanations. Overall $p = 0.002$ for OC− and $p = 0.012$ for OC+.
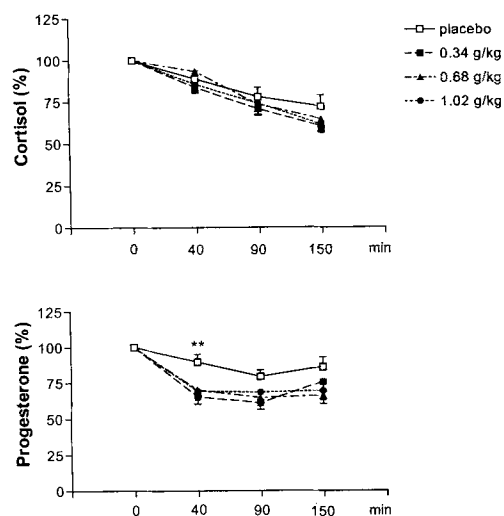

Fig. 3. Relative cortisol and progesterone levels during placebo and different alcohol drinking events in 10 subjects using oral contraceptives (substudy C). **$p < 0.01$ for all doses.

0.02; prolactin $= 4.9 + 0.12 \times$ day, substudy A) and were significantly elevated relative to OC− subjects (substudy B, Table 1). A transient increase in prolactin levels in the beginning of alcohol intoxication relative to placebo was observed. Among OC+ subjects, a significant effect was observed in substudy A ($F = 8.1, p < 0.001$) (Fig. 4, Table 2). Among OC− subjects, an overall significant effect was found with the two substudies combined ($F = 3.2, p = 0.046$; Fig. 4, Table 3).

The baseline LH levels were significantly lower among OC+ subjects than in OC− subjects (Table 1), and a decline was observed at the start of taking the oral contraceptive at day 8 of the menstrual cycle (Fig. 5). No significant effect of alcohol on LH levels was observed among OC− subjects ($F = 1.8, p = 0.17$, Table 3). Among OC+ subjects, a tendency for an overall effect was observed ($F = 2.4, p = 0.11$, Table 2), and in a subanalysis of menstrual cycle days 7–20, levels were significantly lower during alcohol at 120 min (75 ± 10% vs. 112 ± 10%, $p = 0.024$; Fig. 5).

The baseline cortisol levels were significantly higher among OC+ than in OC− subjects (Table 1). The levels did not correlate with the day of menstrual cycle in substudy A ($r = 0.04, p = 0.83$ for OC− and $r = 0.17, p = 0.36$ for OC+). No significant differences in cortisol levels during alcohol and placebo sessions were observed for OC− and OC+ subjects in the separate substudies (Tables 2 and 3, Fig. 3) or with substudies A and B combined ($F = 1.5, p = 0.23$ for OC− subjects; $F = 0.2, p = 0.82$ for OC+ subjects).

DISCUSSION

The present study provides evidence that intake of a low dose of alcohol (about two drinks) is associated with acute changes in hormonal levels in premenopausal women using oral contraceptives as well as among nonusers. This is, to our knowledge, the first presentation concerning the effect of alcohol on the hormone balance in women using oral contraceptives.

That alcohol intake is associated with an acute elevation in plasma estradiol levels in premenopausal women (Väli-mäki et al., 1983; Mendelson et al., 1987, 1988, 1989; Teoh et al., 1988; Teoh et al., 1990, as well as in postmenopausal women on estrogen replacement therapy (Ginsburg et al., 1996), has earlier been demonstrated. Furthermore, estradiol has—in both interventional and cross-sectional studies—been positively associated with alcohol intake (Reichman et al., 1993; Muti et al., 1998; Gavaler and Van Thiel, 1992), providing a possible link between alcohol consumption and breast cancer (Smith-Warner et al., 1998). Our results are in line with the earlier findings, although the elevation in estradiol in the present study was observed primarily among women using oral contraceptives. For women not using oral contraceptives, our results suggest an overall decline and a superimposed elevation during midcycle in response to alcohol intake. The estradiol findings in the present study are strikingly similar to those of an earlier study which found that alcohol intake elevated testosterone in premenopausal women using oral contraceptives, as well as among nonusers during midcycle (Eriksson et al., 1994).

The results from the present study indicate that alcohol intake is associated with an acute decline in progesterone levels among women using oral contraceptives as well as among nonusers, and that the progesterone effect is not

Table 3. Effect of Alcohol (Mean and 95% Confidence Intervals) on Hormone Levels Among Women Not Using Oral Contraceptives (OC−)
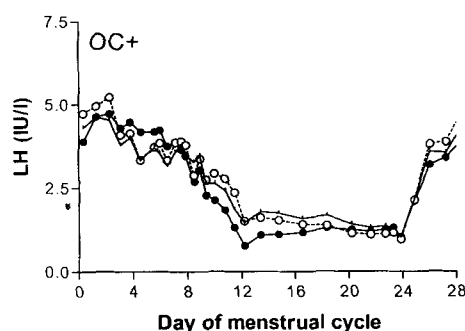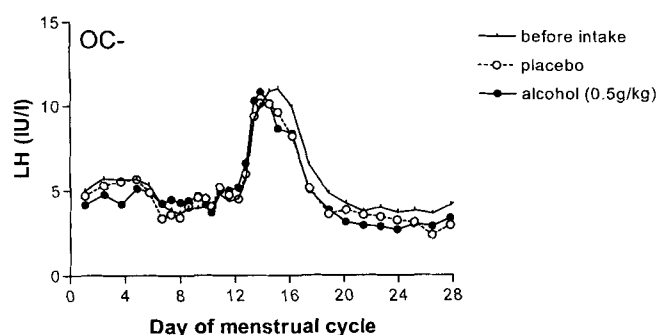
	Time from intake							
	Substudy A				Substudy B			
	60 min		120 min		45 min		90 min	
	Mean	95% CI	Mean	95% CI	Mean	95% CI	Mean	95% CI
Estradiol	−1%	(−9,+7)	−4%	(−12,+5)	−0.4%	(−7,+6)	+0.5%	(−9,+10)
Estrone	ND		ND		+3%	(−6,+12)	+5%	(−3,+12)
Progesterone	−14%	(−22,−6)**	−7%	(−17,+4)	−5%	(−12,+2)	−7%	(−15,+1)
Prolactin	+16%	(−3,+34)	−3%	(−16,+10)	+12%	(−3,+27)	+5%	(−7,+18)
Cortisol	+0.3%	(−9,+9)	−13%	(−20,+4)	−6%	(−14,+3)	−8%	(−22,+7)
LH	+8%	(−4,+19)	−6%	(−22,+9)	ND		ND	

ND = not determined.
** $p < 0.01$ changes during alcohol and placebo conditions compared.
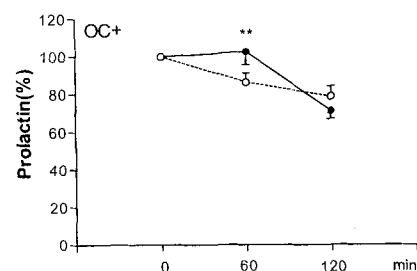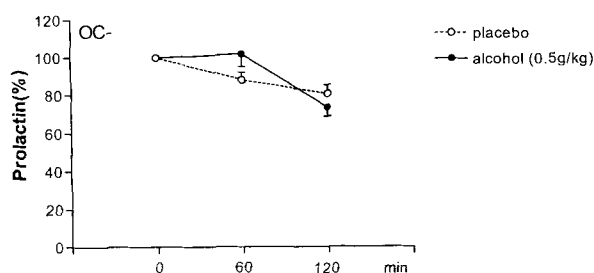
Fig. 4. Relative prolactin levels during placebo- and alcohol-drinking events among 31 subjects using oral contraceptives (OC+) and 30 subjects not using oral contraceptives (OC−) in substudy A. **$p = 0.0048$.

Fig. 5. Luteinizing hormone (LH) levels after intake of placebo or alcohol among 30 subjects not using oral contraceptives (OC−) and 31 subjects using oral contraceptives(OC+) in substudy A. For explanations see legend to Fig. 1.

dose dependent. Earlier studies, with considerably lower statistical power, have demonstrated similar progesterone effects only during stimulatory conditions among premenopausal women not using oral contraceptives (Teoh et al., 1990; Saxena et al., 1990). The levels of sex hormone-binding globulin and albumin to which the major part of the sex steroids are bound were not measured in the present study, because acute changes in these proteins during alcohol intake seem unlikely during the present short time interval.

The elimination of ethanol increases the ratio of NADH to NAD in the liver, and this effect is rather constant during different dose and time conditions of ethanol oxidation (Forsander, 1970). The 17β-hydroxysteroid dehydrogenase type 2 enzyme found in the endometrium and liver preferentially catalyzes the oxidation of 17β-hydroxysteroids (e.g., the catabolic conversion of estradiol to estrone and testosterone to androstenedione) and uses the same cofactor (NAD) as alcohol dehydrogenase (Andersson and Mogh-

rabi, 1997). Furthermore, this isoenzyme has also been found to catalyze the oxidation of 20α-dihydroprogesterone to progesterone (Andersson and Moghrabi, 1997). Thus, our results suggest that the observed increase in estradiol and the estradiol-to-estrone ratio, as well as the decrease in progesterone, are due to the alcohol-induced changes in the redox state leading to a decreased oxidation and/or increased reduction of the steroids in the liver (Fig. 6). A similar effect has been described for conjugated steroids (Andersson et al., 1986). The finding that these effects were most clearly seen among women using oral contraceptives may be explained by the fact that the 17β-hydroxysteroid type 2 enzyme is induced by synthetic progestins found in the contraceptive preparation (Tseng and Gurpide, 1979). It is of interest that the 17β-hydroxysteroid dehydrogenase
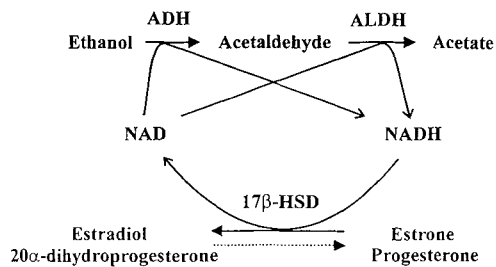
Fig. 6. Coupling of ethanol and sex steroid metabolism in the liver. ADH = alcohol dehydrogenase, ALDH = aldehyde dehydrogenase, NAD = nicotinamide adenine dinucleotide, NADH = reduced form of nicotinamide adenine dinucleotide. 17β-HSD = 17β-hydroxysteroid dehydrogenase. The dashed arrow denotes a decrease in the reaction rate.

type 2 enzyme also has been found to be enriched in breast glandular epithelial cells (Blomquist, 1995). An alcohol-induced redox change in the breast tissue leading to a local increase in estradiol could, in addition to the overall estradiol elevation, provide a link between alcohol consumption and the development of breast cancer.

No acute effect of alcohol on luteinizing hormone levels was observed in the present study among women not using oral contraceptives. However, among women using oral contraceptives, an overall decreasing tendency was found, and in a subanalysis of subjects in the midcycle phase, a significant decline was observed at 120 min from intake. This finding is in contrast to earlier studies that reported that no effects of alcohol had been observed in women or men (McNamee et al., 1979; Mendelson et al., 1981, 1987, 1989; Välimäki et al., 1983; Teoh et al., 1988; Becker et al., 1988; Välimäki et al., 1990). The fact that none of the studies included women using oral contraceptives may well explain this discrepancy. The decline in LH levels may be mediated by a feedback response to the alcohol-induced increase in testosterone among these women (Eriksson et al., 1994).

A transient effect of alcohol on prolactin levels compared with placebo was observed, with a significant elevation at 60 min, followed by a tendency for a decline at 120 min from the start of intake. The smaller differences in the levels in the second substudy indicate that the elevating effect of alcohol is short and that it peaks close to 60 min from the start of drinking. These findings are in line with the earlier studies that found that alcohol elevated prolactin during human chorionic gonadotropin and naloxone stimulation (Mendelson et al., 1987; Teoh et al., 1990). A decline at 2–4 hr from the start of drinking has also been described (Välimäki et al., 1983). The exact mechanism of the prolactin effect cannot be provided by the present data but may involve the opioid peptides and dopamine which participate in the hypothalamic regulation of pituitary prolactin secretion (Tuomisto and Männistö, 1985). The elevation in prolactin levels may thus reflect an activated opioid system, inasmuch as acute alcohol intake has been reported to release β-endorphin peptides in the rat hypothalamus (Gianoulakis, 1990) and elevate plasma

β-endorphin in man (Gianoulakis et al., 1989). The subsequent decline in prolactin levels may, on the other hand, be the result of increased dopaminergic activity in the hypothalamus, as has also been shown to occur in the rat (Ching and Lin, 1994). Baseline prolactin levels were found to be elevated by the use of oral contraceptives, as has been described earlier (Jung-Hoffmann et al., 1988).

No significant effects were observed in cortisol levels during the present dose and time conditions. The finding supports earlier conclusions that an acute effect of alcohol on cortisol levels can mainly be observed only late after the intake of higher doses and may thus be due to withdrawal-induced stress (Ekman et al., 1994).

In conclusion, our results suggest that the acute changes in female sex steroids induced by a low alcohol dose may be mediated by the change in the redox state in the liver. The transient effect of alcohol on prolactin levels may reflect changes in the opioid peptides and dopamine in the hypothalamus. The magnitude of the observed hormonal changes is relatively small, and the physiological significance in an acute situation is not clear. However, our results may provide a mechanism for the association between moderate to heavy alcohol consumption, estrogens, and the development of breast cancer.

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