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Alcohol Effects on Plasma Luteinizing Hormone Levels in Menopausal Women

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MENDELSON, J. H., N. K. MELLO, J. ELLINGBOE AND S. BAVLI. *Alcohol effects on plasma luteinizing hormone levels in menopausal women.* PHARMACOL BIOCHEM BEHAV 22(2)233–236, 1985.—Plasma luteinizing hormone (LH) levels were determined in five healthy post-menopausal adult females prior to, during, and following a period of acute alcohol intoxication. LH levels were also determined in the same women following acute administration of a nonalcoholic beverage which had identical isocaloric value of alcohol. Plasma samples were collected at 30-minute intervals from an indwelling intravenous catheter from 120 minutes prior to alcohol or isocaloric beverage administration to 300 minutes following beverage intake. All women became moderately intoxicated after acute alcohol administration and developed peak blood alcohol levels of 94 mg per dl between 60 to 90 minutes following alcohol intake. LH levels determined before administration of alcohol or isocaloric beverage were not significantly different and were within the range of normal values for healthy, post-menopausal women. No significant differences were found between LH levels following alcohol administration when compared with LH values after isocaloric beverage. These data indicate that acute alcohol intake which produces blood alcohol levels slightly below usual legal limits of intoxication does not suppress LH in post-menopausal females. Since post-menopausal females do not have significant estradiol feedback control of LH secretory activity, and since LH secretory activity in post-menopausal women (in contrast to pre-menopausal females) is more sensitive to the inhibitory actions of drugs which may affect adrenergic and dopaminergic pathways in brain, the findings obtained in this study do not support an acute alcohol effect upon hypothalamic-pituitary modulation of gonadotrophin release in humans.

Alcohol LH Menopausal women

AN association between chronic alcoholism and menstrual irregularities was noted over 160 years ago [18]. Amenorrhea, infertility, miscarriages as well as gynecological problems appeared to be overrepresented in women with alcohol abuse problems [1, 8, 20]. In experimental animal studies relatively high doses of alcohol inhibited estrus rodents [3,5].

Chronic alcohol intake studied under controlled research ward conditions has been shown to suppress plasma testosterone levels in both *alcoholic* and *normal men* [6,10]. Acute alcohol administration to *normal males* was associated with the suppression of plasma testosterone levels without antecedent decrements in LH [12]. LH levels were significantly increased at peak blood levels when testosterone values were lowest. Acute alcohol administration may increase LH levels as a consequence of alcohol induced suppression of testosterone production with subsequent feedback stimulation of LH secretory activity. This interpretation is supported by studies with experimental animals which have demonstrated that alcohol inhibits testicular steroidogenesis [2,4].

Acute alcohol administration to *normal women* was not associated with any significant alterations in plasma LH or estradiol levels [11]. Pituitary LH secretory activity in normal, pre-menopausal females consists of a pulsatile discharge component superimposed upon a small, continuous secretion of the gonadotrophins [22]. Control of the pulsatile release of LH is mediated by intermittent adrenergic signals which stimulates LRF secretory activity which, in turn, induces a pulsatile release of LH from the pituitary [14,21]. Estrogen inhibits the dopaminergic induction of LRF release [7]. In order to control for the influence of estrogen modulation of LH secretion following acute alcohol administration, normal, healthy, post-menopausal women were recruited as subjects for this study. These women do not produce significant amounts of estradiol and hence, LH secretory activity is not modulated by estrogen feedback control.

Another reason for studying post-menopausal females is that LH secretory activity in post-menopausal women is more sensitive to the inhibitory action of drugs which may affect adrenergic or dopaminergic pathways in the brain and hypothalamus. For example, Grossman and his associates [7] have reported that long-acting analogs of met-enkephalin "produced a clear and progressive fall in plasma LH in menopausal women greatly exaggerating the smaller fall we have previously reported in normal subjects" [7]. These data suggested that possible inhibitory effects of ethanol on LH secretory activity would be more readily detected in *post-menopausal* women who did not have estradiol feedback suppression of pulsatile LH release than in normal pre-menopausal females. However, the study of post-menopausal women would not compromise the possibility of

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discovering a potential stimulatory effect of ethanol on LH pulsatile release. Scaglia and his associates [15] have reported that "normal pituitary gonadotrophin function and pituitary reserve and responsiveness to exogenous stimulation are maintained in women of advanced age."

METHOD

Five, healthy, adult females between the ages of 54 and 59 (mean=57) provided informed consent for their participation in these studies. All women reported complete cessation of menstrual periods for a duration of at least one year. None of the women had experienced significant post-menopausal symptoms and none had ever received steroid medication. Prior to cessation of menstruation all reported a history of normal menstrual function and none had any past history of gynecological disease. All subjects had a normal physical and mental status examination as well as normal laboratory blood studies and urinalysis. None had any past or current history of alcoholism or drug abuse.

Each woman served as her own control under conditions of alcohol and isocaloric beverage administration. These two studies were carried out one to three weeks apart.

Subjects reported to the laboratory after a 12-hour fast. All studies were begun at the same time of day (9:00 a.m.). Blood samples were collected from an indwelling intracatheter inserted into the antecubital vein. Specimens were collected at consecutive 30-minute intervals over a 6-hour time period (2 hours before and 4 hours after consumption of an oral dose of alcohol or isocaloric beverage). Alcohol was administered in the form of 100 proof beverage (vodka) in a dose of 2.2 ml per kg body weight diluted in a standard volume (240 ml) of fruit juice. Subjects consumed their alcohol within 15 to 20 minutes and peak alcohol concentrations 94±8 (S.E.) mg/dl were detected 90 minutes after ingestion of alcohol.

Isocaloric beverage consisted of sweetened fruit juice (250 ml) administered after conditions of fasting identical to those following alcohol intake. Three subjects received isocaloric beverage in their first experimental study and alcohol in their second study; two subjects received alcohol in their first experimental study and isocaloric beverage in the second study. During the 6-hour blood collection period subjects were comfortably seated in a reclining chair and were permitted to listen to radio, watch television and read magazines.

Plasma LH concentrations were measured in duplicate 0.100 ml aliquots from each 30-minute plasma sample using a double antibody radioimmunoassay similar to that described for human gonadotrophins [13]. Radio-iodinated LH was purchased from Cambridge Nuclear (Billerica, MA). Anti-LH serum and LH standard (LER-907) were provided by the National Pituitary Agency. Results are expressed as nanograms of LER-907 standard per milliliter of plasma.

RESULTS

Table 1 presents the mean, standard deviation, standard error for plasma LH values obtained at 30-minute consecutive intervals from 120 minutes prior to and 300 minutes following (at 0 time on Table 1) administration of ethanol. Peak blood alcohol levels were achieved between 60 and 90 minutes after ethanol ingestion with mean (±S.E.) values of 94±8 mg per dl. There were no statistically significant changes in plasma LH following alcohol administration (including LH values at peak blood alcohol levels) when these

TABLE 1

PLASMA LH (LER 907-ng/ml) VALUES PRIOR TO (−120 MIN TO 0) AND FOLLOWING (0 TO +300 MIN) ACUTE ALCOHOL INTAKE

Alcohol (N=5)	mean	274.5	258.7	252.7	211.8	222.9	255.7	268.0	257.3	237.0	235.7	250.3	253.4	266.0
	S.D.	79.39	50.58	42.7	48.4	70.6	114.8	94.8	110.8	93.1	78.2	61.3	82.8	46.2
	S.E.	39.70	25.29	21.2	21.7	31.6	51.3	42.4	55.4	41.7	34.9	27.4	37.0	23.1
Control N=5	mean	294.2	274.1	281.2	279.7	233.7	277.8	266.5	274.1	284.0	244.3	268.4	258.7	274.9
	S.D.	111.1	100.6	89.0	103.4	54.0	77.1	98.1	101.4	107.5	82.7	108.5	104.8	86.3
	S.E.	49.7	44.9	39.8	46.2	24.2	34.5	43.9	45.3	48.1	37.0	48.5	46.9	38.6
Time		−120	−90	−60	−30	0	+30	+60	+90	+120	+150	+180	+240	+300

data are compared with pre-alcohol LH. Administration of isocaloric beverage did not produce any significant changes in plasma LH when compared with pre-administration values. There were no statistically significant differences between plasma LH following alcohol administration when compared to values after administration of isocaloric beverage.

DISCUSSION

Data obtained in this study do not support the hypothesis that *acute* alcohol administration suppresses plasma levels of LH in post-menopausal females. The rationale for selection of post-menopausal females (in contrast to pre-menopausal women) as subjects for this study is that these women exhibit enhanced sensitivity to inhibitory drug effects on LH secretory activity [7]. It is important to examine *acute* alcohol effects on female hormones as well as *chronic* ethanol effects for clarifying the role of ethanol as a modulator or pertubator of the hypothalamic-pituitary axis. There is considerable evidence that chronic alcohol abuse and alcoholism is associated with derangements in procreative function and behavior [1, 8, 18, 20] as well as abnormalities in pituitary gonadal hormones [3,5]. However, extrapolation of these derangements in hormonal function to effects of acute or moderate alcohol use is not appropriate.

Since LH levels in post-menopausal women are significantly higher than LH in females prior to cessation of menstrual function, we postulated that any suppressive effects of ethanol upon this hormonal system could be readily detected. In previous studies we have not observed any acute effects of ethanol on LH levels in normally cycling females studied during the late follicular phase of the menstrual cycle [11]. Findings obtained in this study are also in agreement with those of McNamee and his associates [9] who detected no ethanol induced changes in pituitary hormones in normal pre-menopausal females.

The data obtained in this study cannot be readily compared to findings obtained following chronic administration of high doses of ethanol to experimental animals. Van Thiel and his associates [19] provided a diet containing 36 percent of total calories as ethanol for a 56-day consecutive period to female rats and found major derangements in gonadal morphology and function. The duration of alcohol administration to this rodent species is comparable to uninterrupted intake of beverage alcohol which would produce 24-hour blood alcohol levels in excess of 100 mg/dl for 1,186 consecutive days (3.25 years) by human females. Uninterrupted consumption of ethyl alcohol for such a long duration of time would likely produce not only changes in pituitary gonadal hormone function but also induce severe intercurrent toxic and metabolic disorders. Future studies should explore the effects of *chronic* alcohol intake and alcohol abuse on pituitary hormone function in human females.

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