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Moderate alcohol consumption lowers risk factors for cardiovascular disease in postmenopausal women fed a controlled diet[1,2]

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ABSTRACT

Background: Moderate alcohol consumption (1–2 drinks/d) may decrease cardiovascular disease risk in postmenopausal women by improving lipid profiles.

Objective: We measured the effect of moderate alcohol consumption on lipids and lipoproteins in postmenopausal women.

Design: Postmenopausal women ($n = 51$) consumed 0 (control), 15 (1 drink), and 30 (2 drinks) g alcohol (ethanol)/d for 8 wk each as part of a controlled diet in a randomized crossover design. The control diet provided ≈15%, 53%, and 32% of energy from protein, carbohydrate, and fat, respectively. The energy provided from alcohol in the 15- and 30-g alcohol diets was replaced with energy from carbohydrate.

Results: Compared with concentrations after the control diet, plasma LDL cholesterol decreased from 3.45 to 3.34 mmol/L ($P = 0.04$) and triacylglycerol from 1.43 to 1.34 mmol/L ($P = 0.05$) after 15 g alcohol/d. There were no additional significant decreases in either lipid after an increase in alcohol intake from 15 to 30 g/d. Compared with concentrations after the control diet, plasma HDL cholesterol increased nonsignificantly from 1.40 to 1.43 mmol/L after 15 g alcohol/d but increased to 1.48 mmol/L after 30 g alcohol/d ($P = 0.02$). Apolipoprotein A-I increased significantly and apolipoprotein B decreased significantly after 30 g alcohol/d relative to the concentration after the control diet.

Conclusions: Consumption of 15–30 g alcohol/d by postmenopausal women apparently decreases cardiovascular disease risk by improving lipid profiles. Plasma LDL-cholesterol and triacylglycerol concentrations improve after 15 g alcohol/d; plasma HDL cholesterol improves only after 30 g alcohol/d. *Am J Clin Nutr* 2002;75:593–9.

KEY WORDS Alcohol, LDL cholesterol, HDL cholesterol, triacylglycerols, postmenopausal women, triglycerides, cardiovascular disease

INTRODUCTION

A woman's risk of cardiovascular disease increases after menopause, whether the menopause is natural or artificially induced early. For example, the incidence of coronary artery disease in women increases after bilateral oophorectomy (1) or early natural menopause (2). The risk of cardiovascular disease has been linked to decreases in endogenous estrogens after cessation of menses, and hormone replacement therapy has been shown to reduce the incidence of coronary heart disease in postmenopausal women (3). It is proposed that the increase in plasma LDL cholesterol that occurs with and before (4) menopause is a factor associated with the increase in risk of cardiovascular disease. Even more so than an elevated LDL-cholesterol concentration, high HDL cholesterol is an important predictor of a decreased risk of coronary artery disease in women (5, 6). One dietary component that may ameliorate the lipid profile associated with the risk of cardiovascular diseases is moderate alcohol consumption. Alcohol affects both LDL- and HDL-cholesterol metabolism in premenopausal women (7), and data from epidemiologic surveys suggest that alcohol also can decrease the risk of cardiovascular disease in middle-aged women (8, 9). It is critical to determine the effect of dietary components, including alcohol, that modulate blood lipid and lipoprotein concentrations in postmenopausal women because changes in blood lipids and lipoproteins are known risk factors for cardiovascular disease.

HDL-cholesterol-raising and LDL-cholesterol-lowering effects of alcohol were shown in a well-controlled dietary intervention study with premenopausal women (7), but few data exist for postmenopausal women, who are at an increased risk of cardiovascular disease. We showed previously that alcohol does not increase endogenous estrogen in postmenopausal women (10). Thus, if interactions of alcohol and endogenous estrogens are important in mediating the risk of cardiovascular disease, alcohol may have different effects in postmenopausal women than in premenopausal women.

This controlled diet study was designed to establish the effect of moderate alcohol consumption on blood lipid risk factors for cardiovascular disease in postmenopausal women. Data from

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controlled diet studies are critical for formulating public health recommendations because moderate alcohol consumption appears to increase the risk of some diseases (11) and decrease the risk of others (8).

SUBJECTS AND METHODS

Study design

This dietary intervention was designed as a crossover study with three 8-wk treatment periods. During each period, postmenopausal women consumed a controlled diet and were provided a beverage each day that contained 0, 15, or 30 g alcohol (95% ethanol). Each subject completed each of the 3 periods, and the sequence of alcohol treatment for each subject was randomly assigned before the study started. Before each treatment period, there was a 2- to 5-wk period during which the subjects could not consume alcohol but had no other restrictions on food intake.

Subjects

Postmenopausal women were recruited by advertisement from the communities surrounding the Beltsville Human Nutrition Research Center, Beltsville, MD. The subjects were required to *1*) be women ≥50 y of age, *2*) be postmenopausal (last menses ≥12 mo before the study started, follicle-stimulating hormone >40 000 IU/L, natural menopause or hysterectomy with at least one ovary intact), *3*) not be receiving hormone replacement therapy, *4*) not be taking prescription medications that might interfere with the study, *5*) be willing and able to consume the diet prepared or approved by the Center and no other foods or beverages, *6*) have a body mass index between 90% and 140% of ideal, and *7*) have no personal or parental history of alcohol abuse.

The subjects were evaluated by a physician and determined to be in good health with no signs or symptoms of hyperlipidemia, diabetes, peripheral vascular disease, gout, liver or kidney disease, or endocrine disorders.

The study procedures were approved by the National Cancer Institute's Institutional Review Board and the Committee on Human Research of the Johns Hopkins University School of Hygiene and Public Health. All subjects were fully informed of the study requirements and were required to read and sign a consent form detailing the study objectives, risks, and benefits before entry into the study. The subjects were compensated for their participation.

Diets, feeding, and compliance

A 7-d menu cycle of traditional American foods was based on nutrient data from the US Department of Agriculture Nutrient Database for Standard Reference, release 12 (12). Diets were formulated to reflect current average US macronutrient intakes and to provide ≈15% of energy from protein and 33% of energy from fat, with a ratio of polyunsaturated to monounsaturated to saturated fatty acids of 0.6:1:1. The balance of dietary energy was from carbohydrate and alcohol. Diets were formulated to provide ≥100% of the recommended dietary allowances for vitamins and minerals (13). During the study period (including breaks before treatment periods) the subjects were not allowed to consume any vitamin, mineral, or herbal supplements, except for calcium and iron if prescribed by a physician.

During each period of the feeding study, diet composites were collected and chemically analyzed across the menu cycle. One composite of each of the 3 treatments was collected at each of 2 levels of energy. Food for these composites was prepared each day as though it were to be consumed, but instead it was blended and freeze-dried. To prepare a weekly composite, the daily samples were pulverized and 15% of each day's dry weight was mixed. Diets were analyzed for dry matter, crude protein, crude fat, total dietary fiber, ash, cholesterol, and calcium (Covance, Inc, Madison, WI). The fatty acid composition of the food composites was determined after gas chromatographic separation of the fatty acid methyl esters (Covance, Inc).

The amount of alcohol in each treatment was fixed at 0 (control), 15, or 30 g/d for all subjects, independent of their maintenance energy requirement. Alcohol (Everclear; David Sherman Corporation, St Louis) was provided with 340 g orange juice. To compensate for the higher energy content provided by alcohol (29.3 kJ/g), the diets providing 0 and 15 g alcohol were supplemented with carbohydrates (soft drinks and Polycose; Ross Products Division, Abbott Laboratories, Columbus, OH). Because Polycose does not mix well with orange juice, it was added to potatoes or yogurt. Except for the different amounts of alcohol and carbohydrates provided, all subjects were fed the same food items. Therefore, the relative amounts of most nutrients were constant and directly proportional to the energy required to maintain weight. The subjects were instructed to consume their beverage (alcohol or control) with the evening snack food (provided as part of the controlled diet) over a 1- to 2-h period before going to bed and after completing activities requiring substantial manual dexterity, including driving.

Twice during each of the 3 treatment periods, compliance with alcohol intake was determined by adding riboflavin (40 mg) to the alcohol and control beverages. The following morning, the subjects were asked to provide a urine sample. The presence of riboflavin was qualitatively determined by fluorescence under black light. These compliance checks were random and unannounced.

Monday through Friday, the subjects consumed breakfast and dinner at the Beltsville Human Nutrition Research Center's Human Study Facility under the supervision of a dietitian. At breakfast, each subject was provided with a carryout lunch to be consumed that day. Snack items were included in the daily menu and consumed with the evening beverage. Meals for the weekend were packaged for home consumption and provided to the subjects with written instructions after dinner on Friday. Coffee and tea were allowed in unlimited amounts, but sugar and milk were provided with the meals. Non-energy-containing soft drinks were provided ad libitum to be consumed as part of the study meals or for consumption away from the facility. Only foods provided by the Human Study Facility were allowed to be consumed during the study. Each morning, Monday through Friday, the subjects were weighed before breakfast when they arrived at the facility. Energy intake was adjusted in 0.84-MJ (200-kcal) increments to maintain initial body weight.

Each day, the subjects completed a questionnaire detailing beverage intake, factors related to dietary compliance, exercise performed, medications taken, illnesses incurred, and questions or problems with the diets. The questionnaires were routinely reviewed by a study investigator and all problems identified were discussed with the subjects during the next meal. Exercise was not controlled, but subjects were encouraged to maintain their normal exercise patterns (type of exercise, duration, and frequency) throughout the study and to record the type and duration of exercise on their daily questionnaire.

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TABLE 1
Physical characteristics and menopausal history of the subjects at baseline[1]

	Mean (range)
Age (y)	60 (49–79)
Height (cm)	163.7 (152.1–179.7)
Weight (kg)	72.1 (41.3–116.1)
BMI (kg/m^2)	26.9 (17.3–41.8)
Total cholesterol (mmol/L)	5.37 (3.71–7.37)
LDL cholesterol (mmol/L)	3.38 (1.84–5.01)
HDL cholesterol (mmol/L)	1.33 (0.46–2.43)
Triacylglycerol (mmol/L)	1.44 (0.62–3.55)
Apolipoprotein A-I (g/L)	1.79 (1.15–2.80)
Apolipoprotein A-II (g/L)	0.33 (0.11–0.53)
Apolipoprotein B (g/L)	0.91 (0.51–1.49)
Time since cessation of last menses (y)	14 (1–39)
History of hysterectomy (*n*)	8[2]
History of natural menopause (*n*)	43

[1] *n* = 51.
[2] Three subjects had a hysterectomy after natural menopause.

Biological sample collection and analysis

Baseline samples were collected during the week before the controlled feeding began. During the eighth week of the 3 controlled alcohol treatment periods, 2 blood samples were collected, separated by ≥24 h. Procedures for blood sampling and processing were those described in the protocol for the Lipid Research Clinics program (14). Blood samples were drawn after an overnight fast (minimum 12 h), immediately before breakfast.

Plasma was harvested from the whole blood collected by venipuncture in tubes containing EDTA and subsampled into cryogenic vials for storage at −80°C. Before freezing, one subsample was precipitated for HDL measurement with the use of the sequential precipitation procedure of Gidez et al (15). Cholesterol, triacylglycerol, and apolipoprotein (apo) concentrations were analyzed after the final blood collection; all samples for individual subjects were analyzed in the same run.

Lipid analyses were performed at the Lipid Research Clinic Laboratory, The George Washington University Medical Center, which maintains standardization with the Centers for Disease Control and Prevention, US Department of Health and Human Services (Atlanta), for the analysis of total cholesterol, triacylglycerol, and HDL-cholesterol concentrations. Plasma total cholesterol, HDL-cholesterol, and triacylglycerol concentrations were determined enzymatically with commercial kits (Sigma Chemical Co, St Louis) on an Abbott VP analyzer (Abbott Laboratories, North Chicago, IL). LDL-cholesterol concentrations were calculated by using the Friedewald equation (16). Plasma apo A-I and B concentrations were measured by rate nephelometry (ICS Immunochemical analyzer; Beckman, Brea, CA). Apo A-II concentrations were measured by radial immunodiffusion.

Statistical analysis

Statistical analyses were performed with SAS for WINDOWS (version 8; SAS Institute, Inc, Cary, NC). The analytic plan was designed a priori and described a mixed-effects model for analysis of the data (17). For each variable, the mean of the 2 sample measurements taken during week 8 of each feeding period was analyzed with an analysis-of-variance model that included fixed terms for diet (alcohol treatment), period, diet sequence, and a repeated term for subject. The pretreatment (baseline) value of a variable for a subject was used as a covariate, and an interaction term of diet and baseline was used to determine differential effects of diet as a function of the baseline value of the variable. Differences between diets were tested with Tukey's *t* tests. Model terms were deemed significant at $P < 0.05$. Data are presented as least-squares means and SEs.

RESULTS

Subjects

Fifty-three subjects completed the feeding phase of this study. One subject was found to have elevated triacylglycerols (>3.91 mmol/L) and was excluded from the data set. The samples from one treatment period for another subject were inadvertently destroyed. Thus, complete data were analyzed and presented for 51 subjects. The physical characteristics, lipid and apo concentrations, and menopausal history of the 51 subjects at baseline are provided in **Table 1**. The mean age of these 51 subjects was 60 y, and the mean time since cessation of last menses was 14 y. Eight women had undergone hysterectomy (without oophorectomy), including 3 who had completed natural menopause before their surgery. Four women had follicle-stimulating hormone concentrations <40 000 IU/L, the cutoff designated a priori, but had been postmenopausal for several years; there was no other evidence of menses in these women. The mean and range of lipid and lipoprotein concentrations before dietary intervention indicated that, with few exceptions, the subjects were normolipidemic.

Diets

The analyzed composition of the 3 diets is shown in **Table 2**. The data indicate that the 3 diets were consistent with the intended formulated composition. On average, the diets provided ≈15% of energy from protein, ≈48% from carbohydrate, and ≈33% from fat. On average, the daily intake across treatments was 83 g protein, 84 g fat, and 242, 268, and 299 g carbohydrate (including 16 g dietary fiber) from the control, 15-g alcohol, and 30-g alcohol diets, respectively. The average daily cholesterol intake was 0.46 mmol (179 mg). The average daily energy intake for weight maintenance across the 3 treatments was 9.49 MJ (range: 8.79–10.68 MJ). The average percentage of energy from alcohol from the 15-g alcohol beverage was 4.7%, and ranged from 4.1% to 5.1% because of the variation in the amount of energy required to maintain body weight. The percentage of energy from alcohol from the 30-g alcohol beverage was 9.2%

TABLE 2
Composition of the 3 controlled diets[1]

	Alcohol intake (g/d)		
Ingredient	0	15	30
Protein (% of energy)	14.8	14.6	14.5
Carbohydrate (% of energy)	53.0	47.3	42.2
Fat (% of energy)	32.2	33.4	34.1
Alcohol (% of energy)	0.0	4.7	9.2
Ratio of polyunsaturated to monounsaturated to saturated fatty acids	0.7:0.9:1.0	0.8:0.9:1.0	0.8:0.9:1.0
Cholesterol (mmol/MJ)	0.049	0.052	0.048
Dietary fiber (g/MJ)	1.7	1.7	1.7

[1] The average daily energy intake of the subjects was 9.49 MJ.

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TABLE 3
Plasma lipid and lipoprotein concentrations and body weight of postmenopausal women after consumption of a controlled diet providing 3 different alcohol intakes for 8 wk each[1]

	Alcohol intake (g/d)			
	0	15	30	SEE
Triacylglycerol (mmol/L)	1.43[a]	1.34[b]	1.28[b]	0.071
Total cholesterol (mmol/L)	5.49[a]	5.38[a,b]	5.35[b]	0.060
HDL cholesterol (mmol/L)	1.40[a]	1.43[a]	1.48[b]	0.023
LDL cholesterol (mmol/L)	3.45[a]	3.34[b]	3.29[b]	0.053
Apolipoprotein A-I (g/L)	1.80[a]	1.80[a]	1.85[b]	0.022
Apolipoprotein A-II (g/L)	0.342	0.344	0.351	0.0060
Apolipoprotein B (g/L)	0.947[a]	0.935[a,b]	0.917[b]	0.0119
Body weight (kg)	72.2	71.8	71.9	2.31

[1] Least-squares means; n = 51. Means in the same row with different superscript letters are significantly different, $P < 0.05$.

(range: 8.2–10.1%). The range in the percentage of energy from alcohol was a consequence of the fact that the alcohol dose was fixed at 0 (0 g alcohol), 1 (15 g alcohol), or 2 (30 g alcohol) drinks/d and was independent of the energy requirement for weight maintenance. However, because an individual's maintenance energy requirement did not change among treatments, the difference in the percentage of energy from alcohol was consistent within an individual. The qualitative test for alcohol intake provided evidence that all subjects had excellent compliance with consumption of the treatment beverages.

Lipids

Compared with concentrations after consumption of the control diet, plasma total cholesterol, LDL-cholesterol, and triacylglycerol concentrations decreased with the 15-g alcohol diet (**Table 3**). There was no further significant decrease in total or HDL cholesterol after consumption of 30 g alcohol. Plasma LDL cholesterol decreased by 4.6% after the 30-g alcohol diet compared with the concentration after the control diet. Compared with the concentration after the control diet, the 2.1% increase in plasma HDL cholesterol after consumption of 15 g alcohol/d was not significant; however, the 5.4% increase after 30 g alcohol/d was significant. The ratio of LDL to HDL cholesterol decreased with the consumption of 15 g alcohol/d (from 2.64 to 2.49, SEE = 0.13) relative to the value after the control diet. The ratio decreased further after consumption of 30 g alcohol/d (to 2.39).

Although alcohol decreased fasting plasma triacylglycerol concentration in all subjects, the effect of the alcohol was greatest in the subjects with the highest baseline triacylglycerol concentration. Given the mean baseline triacylglycerol concentration (1.44 mmol/L), consumption of 15 and 30 g alcohol/d decreased triacylglycerol concentrations by 5.5% and 9.7%, respectively, compared with the concentration after the control diet. However, in subjects with the lowest baseline triacylglycerol concentration, there was a 3.9% decrease after consumption of 15 g alcohol/d and a 6.9% decrease after consumption of 30 g alcohol/d compared with the concentration after the control diet. In subjects with the highest baseline triacylglycerol concentration, the effect of alcohol was greater: triacylglycerol decreased by 6.5% and 11.6% after 15 and 30 g alcohol/d, respectively, compared with the concentration after the control diet.

Compared with the concentrations after the control diet, the apo A-I concentration did not change after 15 g alcohol/d but increased significantly (by 2.2%) after 30 g alcohol/d. Apo A-I increased by 2.6% after 30 g alcohol/d relative to the concentration after 15 g alcohol/d. There was no effect of alcohol consumption on apo A-II concentrations. The mean apo A-II concentration across all diets was 0.346 g/L. The apo B concentration after consumption of 15 g alcohol/d was not significantly different from that after the control diet but decreased (by 3.7%) after consumption of 30 g alcohol/d relative to the concentration after the control diet. However, the apo B concentration after 30 g alcohol/d was not significantly different from that after 15 g alcohol/d.

DISCUSSION

The results of this well-controlled dietary intervention showed that moderate consumption of alcohol (1–2 drinks/d) decreased LDL-cholesterol, apo B, and triacylglycerol concentrations and increased HDL-cholesterol and apo A-I concentrations in postmenopausal women. These observations are consistent with a decreased risk of cardiovascular disease. It was shown previously that a 0.26-mmol/L increase in HDL cholesterol in women is associated with a 32–42% decrease in the risk of coronary artery disease (18, 19). Applying this risk estimate to the magnitude of lipid changes observed in the current study could indicate that consumption of 1 drink/d potentially decreases the risk by 4–5%, and consumption of 2 drinks/d potentially decreases the risk by 10–13%.

Establishing the effect of alcohol on the risk of cardiovascular disease in women is important because the risk increases after menopause. For example, artificial (1) and natural (2) early menopause increase the risk of coronary artery disease, whereas estrogen replacement decreases this risk (3). Although LDL cholesterol is an important risk factor for cardiovascular diseases, and circulating amounts increase after menopause (20, 21), it is thought that HDL cholesterol may be a stronger predictor of risk in women, at least for coronary artery disease (6, 22). The plasma HDL-cholesterol concentration increased after alcohol consumption in the postmenopausal women in the present study, especially at the level of 30 g alcohol (2 drinks)/d.

Interpretation of the existing literature on the effect of alcohol on lipids and lipoproteins is hampered by the wide variability in study designs and populations studied. Most studies of controlled alcohol intake have been conducted in men, with generally consistent findings: HDL cholesterol increases as alcohol intake increases (23). In comparison, there is a paucity of data collected on women, especially postmenopausal women (24). Many studies designed to evaluate the role of alcohol on lipid response fail to control known factors that influence lipids and lipoproteins, particularly diet composition. In many alcohol intervention studies, the subjects are free-living with no dietary restrictions. Clearly, dietary fat, fatty acids, carbohydrate, and other components have a significant influence on circulating cholesterol and triacylglycerol concentrations. In addition, very short intervention periods in many studies of alcohol intake may be insufficient to observe a change in steady state cholesterol concentrations (25).

The effects of alcohol on plasma LDL and HDL cholesterol observed in this study of postmenopausal women are generally consistent with the effects observed in premenopausal women (7, 26). However, it appears that the magnitude of the response to alcohol is less in postmenopausal women than in premenopausal

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women. In premenopausal women who consumed 30 g alcohol/d, the LDL-cholesterol concentration decreased by 8% from the value observed after consumption of a control diet with no alcohol (7); in postmenopausal women who consumed an equivalent amount of alcohol, the LDL-cholesterol concentration decreased by 5%. Similarly, the HDL-cholesterol concentration increased by 10% in premenopausal women who consumed 30 g alcohol/d compared with a 5% increase in postmenopausal women. Thus, although the pattern of change for LDL and HDL cholesterol was similar, alcohol may not modulate plasma lipoproteins in postmenopausal women to the same degree as in premenopausal women consuming similar diets and amounts of alcohol. The benefits with regard to prevention of cardiovascular disease, however, may be substantial and important to postmenopausal women, who are known to be at increased risk.

The magnitude of the effect of alcohol on apolipoprotein concentrations may also be less pronounced in postmenopausal women than in premenopausal women. Clevidence et al (7) found that the apo A-I concentration increased by 8% in premenopausal women compared with 3% in postmenopausal women in the present study after both groups consumed 30 g alcohol/d. When Rumpler et al (26) fed the equivalent of 1 drink/d to women (mixed population of pre- and postmenopausal women with and without hormone replacement), the apo A-I concentration increased by only 2%, which was not a significant change compared with the value after the control diet. Similarly, in postmenopausal women who consumed 1 drink/d, the apo A-I concentration increased by <1% (also not a significant change relative to the value after the control diet). Thus, it appears that 15 g alcohol/d may not be sufficient to elicit a change in apo A-I concentrations, and the change in apo A-I concentrations after 30 g alcohol/d may not be as great in postmenopausal women as in premenopausal women. Alcohol-related changes in apo A-II concentrations have not been observed in postmenopausal women but have been observed in premenopausal women. The nonsignificant 3% increase in the apo A-II concentration in the postmenopausal women consuming 30 g alcohol/d is not as large as the significant (4%) increase observed in premenopausal women. Changes in apo A-I and apo A-II concentrations also suggest that apo A-I is more responsive to alcohol than is apo A-II. This observation is similar to that shown in men, in whom changes in apo A-I concentrations are greater than those in apo A-II in response to alcohol (27). These changes in apo A-I and apo A-II concentrations are consistent with the hypothesis that an increase in the transport rate of these major HDL apolipoproteins is a mechanism by which plasma HDL concentrations increase in response to alcohol consumption (28). Moreover, apo B, the major protein of LDL, decreases in a pattern similar to that of LDL cholesterol and may be a consequence of the apparent impairment of apo B synthesis by alcohol (29). However, the magnitude of the change in apo B was not as great as that in LDL cholesterol. In premenopausal women, LDL-cholesterol concentrations decrease and apo B concentrations remain unaffected (7).

In contrast with the similar effects of alcohol on LDL and HDL cholesterol seen in premenopausal and postmenopausal women, our data suggest that the effect of alcohol on fasting triacylglycerol concentrations may differ by menopause status. Data from the present study with postmenopausal women showed a decrease in triacylglycerol concentrations in response to alcohol intake. In a previous study with premenopausal women, triacylglycerol concentrations did not change in response to alcohol (2 drinks/d) (7) despite a similar diet composition (replacement of energy derived from alcohol with that from carbohydrate) and study design in both studies. Although high alcohol intake leads to hypertriglyceridemia, the response to moderate alcohol intake seems more variable. Clevidence et al (7) did not observe a change in triacylglycerol concentrations in premenopausal women who consumed 2 drinks/d, and Rumpler et al (26) did not observe an effect of alcohol on triacylglycerol concentrations in a mixed population of pre- and postmenopausal women who consumed ≈2 drinks/d. In some uncontrolled diet studies, triacylglycerol concentrations increased after alcohol consumption (30). On the other hand, a stratified random sample of English women aged 25–69 y who consumed moderate amounts of alcohol (1–20 g/d) had lower plasma triacylglycerol concentrations than did nondrinkers in a cross-sectional study of the population (31). Triacylglycerol concentrations are higher in drinkers consuming 60–80 g/d but inconsistent at lower intakes (32). There are also sex differences in the response of triacylglycerol to alcohol. In a comparison of drinkers and nondrinkers, male drinkers had higher triacylglycerol concentrations, but female drinkers did not (33).

The reasons for the discrepancies in triacylglycerol metabolism between men, premenopausal women, and postmenopausal women are not clear, but the data suggest that changes associated with menopause may mediate the triacylglycerol response to alcohol. In premenopausal women, alcohol increases circulating estrogens (34); this increase was not observed in postmenopausal women in another study (10). The triacylglycerol concentration–lowering effect of alcohol observed in postmenopausal women may be masked in premenopausal women by the alcohol-mediated increase in estrogens and consequent increase in triacylglycerol concentrations (35–37).

A confounding issue in determining the effects of alcohol on fasting plasma triacylglycerol concentrations in the present study was the replacement of energy from alcohol with energy from carbohydrate. Although changes in the carbohydrate content of the diet can change fasting plasma triacylglycerol concentrations, many studies (usually confounded with changes in fat content) have reported no change in triacylglycerol concentrations after moderate (8–10% of energy) changes in carbohydrate (38–42). Furthermore, many studies indicate that the effect of the dietary fatty acid composition on fasting triacylglycerol concentrations may be as important as that of carbohydrate, if not more so (43). An 8% energy replacement of carbohydrate for fat from oleic, *trans*, stearate, or saturated fatty acids does not alter fasting plasma triacylglycerol concentrations. However, at a given intake of dietary fat, oleic acid lowers and stearic acid raises fasting plasma triacylglycerol concentrations. Thus, the type of fatty acid used as a replacement may be more important than the amount of fat replaced with carbohydrate, especially when the amount replaced is moderate (8–10% of energy). Similar results were found by Weisweiler et al (39), who replaced energy from polyunsaturated fatty acids with energy from saturated fatty acids. Additional studies are needed to elucidate the effects of carbohydrate and alcohol on fasting plasma triacylglycerol concentrations.

In this study, 0, 15, and 30 g alcohol/d (0, 1, and 2 drinks/d, respectively) were provided to the subjects to establish, at moderate intakes, whether or not there is a response to increasing alcohol intakes or whether there is a threshold for the response. In postmenopausal women, it appears that only 1 drink/d is needed to elicit the benefit from decreases in plasma LDL-cholesterol

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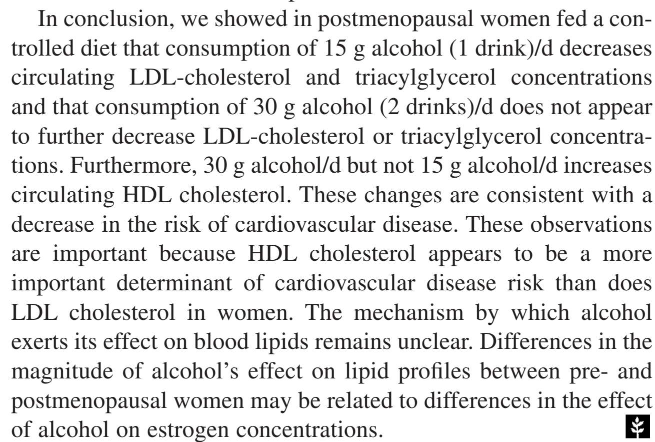
and triacylglycerol concentrations, but 2 drinks/d are needed to elicit the benefit of an increase in HDL cholesterol. Our findings of increases in plasma HDL-cholesterol and apo A-I concentrations with increasing alcohol intakes are consistent with the findings of a meta-analysis of 25 studies (24), although the magnitude of change between the control diet and 30 g alcohol/d in our well-controlled study was about one-half that of the predicted changes based on the meta-analysis: HDL cholesterol increased by 5.4% and the predicted increase was 8.3%, apo A-I increased by 2.7% and the predicted increase was 6.5%. On the basis of the meta-analysis, consumption of 30 g alcohol/d (equivalent to 2 drinks/d) would be predicted to increase triacylglycerol concentrations 5.9% over baseline. In our well-controlled study of moderate alcohol consumption, triacylglycerol concentrations decreased, consistent with cardiovascular disease protection.



In conclusion, we showed in postmenopausal women fed a controlled diet that consumption of 15 g alcohol (1 drink)/d decreases circulating LDL-cholesterol and triacylglycerol concentrations and that consumption of 30 g alcohol (2 drinks)/d does not appear to further decrease LDL-cholesterol or triacylglycerol concentrations. Furthermore, 30 g alcohol/d but not 15 g alcohol/d increases circulating HDL cholesterol. These changes are consistent with a decrease in the risk of cardiovascular disease. These observations are important because HDL cholesterol appears to be a more important determinant of cardiovascular disease risk than does LDL cholesterol in women. The mechanism by which alcohol exerts its effect on blood lipids remains unclear. Differences in the magnitude of alcohol's effect on lipid profiles between pre- and postmenopausal women may be related to differences in the effect of alcohol on estrogen concentrations.

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