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Sex Differences in the Response of Postprandial Lipemia to a Change from a Low-Fat Low-Cholesterol Diet to a High-Fat High-Cholesterol Diet

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Summary

To determine whether a short-term change in dietary habits affects postprandial lipemia in men and women in the same way, postprandial triglyceridemia was measured in age- and BMI-matched young healthy men and women after two weeks on the self-selected low-fat low-cholesterol (LF) diet and after another two weeks on the self-selected high-fat high-cholesterol (HF) diet. After a standardized challenge meal (1.4 g fat/kg of body weight), men had higher postprandial triglyceridemia than women on the HF diet but no such difference was observed on the LF diet. The results of this preliminary study suggest that there may be important sex differences in the mechanisms regulating the postprandial lipemia response to different diets, women being able to adapt better to the HF diet with respect to postprandial lipemia.

Key words

Postprandial lipemia • Plasma triglycerides • Gender

Introduction

Over the past few years, a large body of evidence has accumulated suggesting that exaggerated and prolonged postprandial lipemia is associated with accelerated development of coronary heart disease (for review see Karpe and Hamsten 1995). Therefore, increased attention has been paid to factors affecting the magnitude of postprandial lipemia. It was shown that the extent of postprandial lipemia is affected, among many other factors, by the diet composition (for review see Lairon 1996, Bergeron and Havel 1997) and gender (Cohn *et al.* 1988). However, it is not as yet known whether there are any gender differences in the regulation of the postprandial lipemia response to the diet. Therefore, our preliminary study was designed to establish whether a short-term significant change in dietary habits affects postprandial lipemia equally in men and women. For that reason, postprandial lipemia occurring after a standardized challenge meal was measured in age- and body mass index (BMI)-matched young healthy men and women after two weeks on the self-selected low-fat low-cholesterol (LF) diet and, after another two weeks, on the self-selected high-fat high-cholesterol (HF) diet.

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Method

Five young non-obese men and five age- and BMI-matched women were studied (age: 32±6 and 32±6 years; BMI: 22.7±1.7 and 22.3±2.0 kg/m^2, respectively). At the start of the study, the subjects were normolipemic (cholesterol <5.6 mmol/l, triglycerides <2.2 mmol/l). As determined by the polymerase chain reaction (Eiklid and Leren 1993), four men and three women were found to have the apolipoprotein (apo) E 3/3 genotype, one man apo E 3/4 and two women apo E 2/4.

For two weeks, the subjects consumed the self-selected low-fat low-cholesterol (LF) diet and, for the next two weeks, the self-selected high-fat high-cholesterol (HF) diet. Before each dietary period, the subjects were given very detailed dietary instructions. For the LF dietary period, they were instructed to decrease total fat intake and, when using fats, to select fats of plant origin (margarines and oils). For the HF dietary period, they were instructed to increase total fat intake and to use fats of animal origin (butter). To ensure a high cholesterol intake on the HF diet, three eggs were supplemented to the diet daily.

Table 1. Composition of diets used in the present study.

	Sex	LF diet	HF diet
Energy intake (kJ/day)	Men	10900 ± 1791*	15243 ± 2490*$^{\$}$
	Women	7724 ± 1285	10623 ± 1598†
Energy intake/weight (kJ/day/kg)	Men	141.4 ± 26.4	197.1 ± 36.0$^{\$}$
	Women	126.8 ± 32.2	172.8 ± 33.1†
Protein (% of energy)	Men	13.6 ± 2.5	14.1 ± 1.0
	Women	12.9 ± 3.4	14.7 ± 1.1
Carbohydrate (% of energy)	Men	54.0 ± 7.5	42.8 ± 5.5$^{\#}$
	Women	56.7 ± 6.0	42.9 ± 4.8$^{\#}$
Fat (% of energy)	Men	31.1 ± 8.1	39.0 ± 5.2$^{\$}$
	Women	29.9 ± 5.0	41.0 ± 4.8$^{\#}$
Animal fat (% of energy)	Men	15.2 ± 6.6	32.5 ± 5.7$^{\#}$
	Women	9.9 ± 3.2	32.3 ± 3.8$^{\#}$
Vegetable fat (% of energy)	Men	15.8 ± 4.4	6.5 ± 2.1$^{\#}$
	Women	20.0 ± 6.5	8.7 ± 2.5$^{\#}$
Alcohol (% of energy)	Men	1.3 ± 1.7	4.1 ± 5.1
	Women	0.5 ± 0.7	1.4 ± 2.0
Cholesterol (mg/day)	Men	242 ± 113*	1656 ± 271**$^{\#}$
	Women	102 ± 16	1100 ± 156$^{\#}$
Cholesterol (mg/1000 kJ/day)	Men	21.9 ± 8.3	110.5 ± 23.2$^{\#}$
	Women	13.3 ± 1.6	106.9 ± 30.1$^{\#}$

*Values are means ± S.D. * $p<0.05$, ** $p<0.01$ (men versus women by the unpaired t-test); $^{\$}$ $p<0.10$, † $p<0.05$, $^{\#}$ $p<0.01$ (LF versus HF diet by the paired t-test).*

The composition of the diets was monitored by five-day dietary records at the end of each dietary period (the consumption was recorded on three working and two weekend days). The weight of the subjects was not followed during the study.

On the last day of each dietary period, a fasting blood sample was obtained from each of the subjects (basal samples). The subjects then received breakfast standardized according to their weight at the beginning of the study, a meal of identical composition being provided on both occasions. The breakfast consisted of tea, rolls, ham and a liquid cream (33 % of fat) as the main source of fat. It contained 1.4 g fat, 0.9 g carbohydrate, 0.6 g protein, and 4 mg cholesterol per kg of body weight (total

78 kJ/kg of body weight). The time when breakfast was finished was taken as zero and venous blood samples were then withdrawn in 90-min intervals for 9 h (1.5, 3, 4.5, 6, 7.5 and 9 h).

Plasma triglycerides (TG), cholesterol, and high-density lipoprotein-cholesterol (HDL-cholesterol) were measured using commercially available enzymatic kits (Boehringer, Mannheim, Germany). Apolipoprotein B and A-I in the plasma were determined turbidimetrically with antibodies purified from commercially available goat antisera (ÚSOL, Prague, Czech Republic). The concentration of cholesterol in low-density lipoprotein (LDL-cholesterol) in basal samples was calculated using Friedewald's formula.

The area under the curve of triglycerides (AUC TG) and the area under the increment curve of triglycerides (AUIC TG) during postprandial lipemia as well as the AUC and AUIC of HDL-cholesterol were calculated using the trapezoidal rule.

The data are presented as means ± S.D. Statistical analysis was performed using the BMDP PC 90 statistical package.

Table 2. Effects of LF and HF diets on basal values of the lipid parameters studied.

	Sex	LF diet	HF diet
Triglycerides (mmol/l)	Men	0.96 ± 0.16	1.15 ± 0.35
	Women	1.07 ± 0.41	0.90 ± 0.80
Cholesterol (mmol/l)	Men	4.05 ± 0.28	4.38 ± 0.41*
	Women	4.70 ± 0.69	5.30 ± 0.62†
LDL-cholesterol (mmol/l)	Men	2.67 ± 0.24	2.88 ± 0.39
	Women	2.66 ± 0.51	3.18 ± 0.43†
HDL-cholesterol (mmol/l)	Men	0.94 ± 0.13**	0.98 ± 0.11**
	Women	1.55 ± 0.38	1.78 ± 0.35$^{\#}$
Apo B (g/l)	Men	0.89 ± 0.11	0.96 ± 0.05
	Women	0.75 ± 0.19	0.86 ± 0.16
Apo A-I (g/l)	Men	1.15 ± 0.10	1.17 ± 0.17
	Women	1.24 ± 0.12	1.25 ± 0.10

*Values are means ± S.D. * $p<0.05$, ** $p<0.01$ (men versus women by the unpaired t-test); † $p<0.05$, $^{\#}$ $p<0.01$ (LF versus HF diet by the paired t-test).*

Results

As expected, the diet composition changed markedly between both dietary periods (Table 1). The consumption of fats rose from 31 % on the LF diet to 40 % on the HF diet at the expense of carbohydrate consumption which decreased from 55 % to 43 %. Moreover, the proportion of fats of animal origin more than doubled on the HF diet; simultaneously, there was more than a twofold decrease in the proportion of vegetable fat. Furthermore, the consumption of dietary cholesterol rose markedly on the HF diet. The change from the LF to the HF diet was accompanied by an almost 40 % increase in total energy intake. Importantly, no significant difference between men and women was observed in the diet composition on both the LF and HF diets.

As was anticipated, the change from the LF to the HF diet increased basal cholesterolemia, although this increase was statistically significant in women only (Table 2). The more pronounced increase in women results from an increase in both LDL- and HDL-cholesterol. Importantly, with the exception of HDL-cholesterol on both diets and cholesterolemia on the HF diet, there were no differences in the lipid parameters between the two sexes.

The course of postprandial triglyceridemia evaluated by analysis of variance for repeated measures with two grouping factors (sex and diet) did not differ in both sexes on the LF diet. On the other hand, men

displayed higher postprandial triglyceridemia on the HF diet ($p<0.05$). The difference between both sexes in the course of postprandial triglyceridemia remained significant even after subtraction of basal triglyceridemia ($p<0.05$) (Fig. 1).

Similarly, there was no difference between both sexes in AUC TG and AUIC TG on the LF diet. On the HF diet, both AUC TG and AUIC TG were higher in men, although the difference is significant for AUIC TG only (Table 3). When the effect of the change from LF to HF diet is compared, both AUC TG and AUIC TG tended to increase in men and to decrease in women, although the result is statistically significant for AUC TG in women only (Table 3). Moreover, when individual differences between AUC and AUIC on both diets (Δ_{AUC} = AUC TG[HF] – AUC TG[LF], Δ_{AUIC} = AUIC TG[HF] – AUIC TG[LF], respectively) are compared, the response of both sexes to the diet change differs significantly (Table 3).

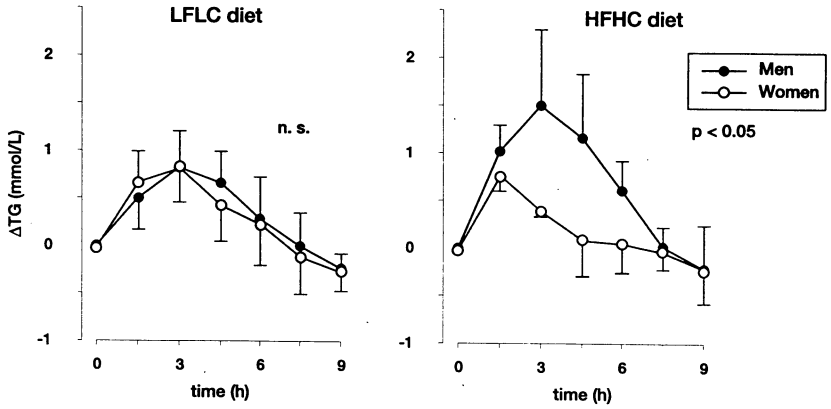

Fig. 1. *Changes in plasma triglycerides in men and women on LF and HF diets. Data are presented as means ± SD. P value was obtained by analysis of variance for repeated measures with two grouping factors (sex and diet).*

Table 3. Effects of LF and HF diets on the magnitude of postprandial triglyceridemia and HDL-cholesterolemia expressed as the area under the curve (AUC) and the area under the increment curve (AUIC).

	Sex	LF diet	HF diet	Δ (HF-LF)
AUC TG (9 h.mmol/l)	Men	+11.9 ± 2.1	+16.5 ± 4.7	+4.7 ± 4.2**
	Women	+12.6 ± 5.6	+9.9 ± 6.2$^{\#}$	–2.7 ± 2.1
AUIC TG (9 h.mmol/l)	Men	+3.2 ± 2.6	+6.2 ± 1.9**	+3.0 ± 1.2*
	Women	+2.9 ± 2.4	+1.8 ± 1.4	–1.1 ± 3.8
AUC HDL-cholesterol (9 h.mmol/l)	Men	+7.9 ± 1.2**	+8.0 ± 0.6***	+0.1 ± 0.7**
	Women	+13.6 ± 2.6	+16.6 ± 3.2†	+3.1 ± 1.7
AUIC HDL-cholesterol (9 h.mmol/l)	Men	–0.5 ± 0.9	–0.8 ± 0.5*	–0.3 ± 0.9
	Women	–0.4 ± 1.1	+0.7 ± 1.2	+1.0 ± 1.9

*Values are means ± S.D. * $p<0.05$, ** $p<0.01$, *** $p<0.001$ (men versus women by the unpaired t-test); † $p<0.05$, $^{\#}$ $p<0.01$ (LF versus HF diet by the paired t-test).*

It is of interest that both AUC TG and AUIC TG correlated negatively with HDL-cholesterol on the HF diet ($r = –0.686$, $p<0.05$; $r = –0.706$, $p<0.05$, respectively) but not on the LF diet ($r = –0.172$, $r = –0.190$, respectively).

As could have been anticipated, AUIC HDL-cholesterol, reflecting the accumulation of cholesterol in HDL in the postprandial phase, was negative in both sexes on the LF diet. On the other hand, AUIC HDL-cholesterol on the HF diet diverged significantly in both sexes reaching positive values in women (Table 3). The same trend was suggested by analysis of variance for repeated measures with two grouping factors (sex and diet) ($p<0.10$).

Discussion

The change from the LF to the HF diet in young healthy volunteers differs in the magnitude of postprandial lipemia in both sexes. While there were no differences in the course of postprandial triglyceridemia between men and women on the LF diet, men displayed higher triglyceridemia on the HF diet.

One might object that self-selected diets cannot be sufficiently controlled. However, there is no other way of explaining the notable increase in cholesterolemia observed in the study than by a principal change in the diet as evaluated on the basis of dietary records. It should be stressed that the purpose of the study was to look at the effect of a major change in the diet by manipulating both quantity and the quality of fat in order to ascertain whether there are indeed any differences between the two genders.

With regard to the potential clinical implications of our results, it is of interest that the LF diet is close to that recommended for the general population and, on the contrary, the HF diet rather corresponds to the Western type of diet associated with higher risk of vascular diseases.

It has been reported that postprandial triglyceridemia tends to be higher in men than in women (Cohn *et al.* 1988). We could not see such a difference on the LF diet, but this was indeed the case on the HF diet. Although there are no data available, we can speculate that the composition of the usual diet of volunteers in the above study was somewhere between our very extreme diets.

It can be hypothesized that the higher postprandial triglyceridemia in men on the HF diet can be explained by a higher rate of production of triglyceride-rich lipoproteins. It has been shown that the increase in postprandial triglyceridemia is due to an increase in triglyceride-rich lipoproteins of both intestinal and hepatic origin (chylomicrons and very low density lipoproteins – VLDL, respectively) (Cohn *et al.* 1993, Schneeman *et al.* 1993). McKeigue *et al.* (1993) showed that the suppression of plasma nonesterified fatty acid concentration induced by the oral glucose tolerance test is more pronounced in women than in men. This might result in a lower rate of VLDL production during the postprandial phase and, therefore, lower postprandial triglyceridemia in women. It is not quite clear as yet why this should be the case on the HF but not on the LF diet.

Another possible explanation for the higher postprandial triglyceridemia in men on the HF diet might be due to delayed catabolism of triglyceride-rich lipoproteins. The activity of lipoprotein lipase, the key enzyme involved in the catabolism of triglyceride-rich lipoproteins, is higher in women than in men (Huttunen *et al.* 1976). However, to the best of our knowledge, there are no data available on sex and diet interaction with respect to lipoprotein lipase activity. The first results emerging from our ongoing follow-up project suggest that young women given isocaloric low-fat or high-fat diets for 4 weeks have lower postprandial triglyceridemia and higher lipoprotein lipase activity (evaluated as the k2 rate constant in the intravenous fat tolerance test) on the high-fat diet (Kovář and Poledne, unpublished results). If this is the case, then higher lipoprotein lipase activity in women on the HF diet could also explain HDL-cholesterol accumulation in the postprandial phase as observed in the present study. Thus the surface components of triglyceride-rich lipoproteins (free cholesterol, phospholipids and apolipoproteins) are released during their hydrolysis by lipoprotein lipase and transported to HDL (Eisenberg 1984). Nevertheless, we do not have any explanation why the differences in lipoprotein lipase activity between both sexes should be affected by the diet.

It is also possible that sex differences in lipoprotein lipase activity do not affect postprandial lipemia when dietary fat intake is low. However, when the fat intake is increased on the HF diet, the capacity of lipoprotein lipase to hydrolyze triglycerides might become a rate-limiting factor in men resulting in higher postprandial triglyceridemia. This could also explain the observed increase in HDL-cholesterol in women but not in men, who might be unable to increase the rate of HDL-cholesterol production on the HF diet. Moreover, such a conclusion could be supported by the observed negative correlation between AUC and AUIC TG on the one hand, and basal HDL-cholesterol on the other hand on the HF diet but not on the LF diet.

It should be kept in mind that the results of our study concerning women could be affected by the menstrual cycle. We did not check for this, but Wendler *et al.* (1992) did not observe any effect of the menstrual cycle on postprandial lipemia.

It can also be objected that the concentration of HDL-cholesterol in men in our present study is quite low and this might affect the magnitude of postprandial lipemia as suggested by Patsch *et al.* (1983). However, the low HDL-cholesterol concentration in men is likely to be related to their low total cholesterol. Moreover, O'Meara *et al.* (1992) showed that not basal HDL-cholesterol, but the triglyceride level is the major determinant of the magnitude of postprandial lipemia.

Prolonged and exaggerated postprandial lipemia has been repeatedly found to be associated with accelerated atherogenesis (for review see Slyper 1992, Karpe and Hamsten 1995). We believe that the better adaptation of young women to the HF diet with respect to postprandial lipemia may be another important factor contributing to their greater protection against cardiovascular diseases.

In conclusion, our results suggest that the response of postprandial triglyceridemia to the HF diet, but not to the LF diet, differs in both genders with men displaying higher triglyceridemia on the HF diet. The preliminary character of our results does not allow us to make any conclusions about the mechanisms responsible for such sex differences. A better controlled study on a larger number of subjects would be required to confirm our results. Such a study would help to improve our understanding of the mechanisms responsible for the better protection of young women against cardiovascular diseases.

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Reprint requests

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