

Original

# Postprandial lipaemia and endothelial adhesion molecules in pre- and postmenopausal Spanish women

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Abstract

**Background:** Postprandial hyperlipaemia is an independent risk factor for atherosclerosis.

**Objectives:** To compare postprandial lipaemia and fasting adhesion molecules levels in healthy young premenopausal (PrW) and postmenopausal (PoW) Spanish women.

**Subjects and methods:** Twenty healthy PrW and 18 healthy PoW participated in a postprandial 7-hour intervention study. All participants were given a fat-rich standard meal (11.8% saturated, 39.7% monounsaturated, and 6.6% polyunsaturated) after a 12 h fast. Blood samples were taken at baseline and at 60, 120, 240, 360 and 420 min after eating. Triacylglycerols (TAG), total cholesterol (Chol), soluble intercellular adhesion molecule-1 (sICAM-1) and soluble vascular adhesion molecule-1 (sVCAM-1) were determined in fasting serum samples and TAG and total Chol postprandial levels were measured.

**Results:** Anthropometric data, serum lipid and sICAM-1 presented significant higher values in PoW compared to PrW, but sVCAM-1 did not significantly differ between groups. Postprandial TAG and Chol concentrations in PoW were significantly higher than in PrW ( $p < 0.0001$ ). There was a significant time influence ( $p < 0.0001$ ) in TAG in PrW and PoW, while time to peak and peak concentration were significantly higher in PoW than PrW. Chol concentrations showed a significant reduction after 1 h, to reach values similar to baseline after 6 h in PrW but not in PoW.

**Conclusions:** Lipid postprandial response to a fat rich meal and soluble intercellular adhesion molecules concentrations indicate a higher cardiovascular risk pattern in postmenopausal compared to premenopausal women. Soluble vascular adhesion molecule levels seem to be influenced not only by age and menopause, but also other factors like usual diet.

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## LIPEMIA POSTPRANDIAL Y MOLÉCULAS DE ADHESIÓN ENDOTELIAL EN MUJERES ESPAÑOLAS PREMENOPÁUSICAS Y POSTMENOPÁUSICAS

Resumen

**Introducción:** La hiperlipemia postprandial es un factor independiente de riesgo de aterosclerosis.

**Objetivos:** Comparar la lipemia postprandial y concentraciones en ayunas de moléculas de adhesión en mujeres sanas, jóvenes premenopáusicas (PrW) y postmenopáusicas (PoW).

**Sujetos y métodos:** 20 PrW y 18 PoW participaron en un estudio de intervención postprandial de 7 horas. Tras 12 horas de ayuno, las participantes tomaron una comida estándar rica en grasa (11,8% saturada, 39,7% monoinsaturada y 6,6% poliinsaturada). Se tomaron muestras de sangre basal y a los 60, 120, 240, 360 y 420 min después de comer. En las muestras en ayunas se determinaron triglicéridos (TAG), colesterol total (Chol), moléculas solubles de adhesión intercelular-1 (sICAM-1) y moléculas solubles de adhesión vascular-1 (sVCAM-1). Asimismo se determinaron TAG y Chol postprandiales.

**Resultados:** Los valores antropométricos, lípidos y sICAM-1 presentaron valores significativamente mayores en PoW frente a PrW, pero sVCAM-1 fueron similares en ambos grupos. Las concentraciones postprandiales de TAG y Chol fueron significativamente mayores en PoW que en PrW ( $p < 0,0001$ ). Hubo un efecto significativo del tiempo en los TAG de PoW y PrW ( $p < 0,0001$ ), mientras que el tiempo para alcanzar la concentración máxima y dicha concentración fueron significativamente mayores en PoW que en PrW. Las concentraciones de Chol mostraron una reducción significativa después de 1 h para recuperar valores similares a los basales después de 6 h en PrW pero no en PoW.

**Conclusiones:** La respuesta lipídica postprandial a una comida rica en grasa y las concentraciones de las moléculas solubles de adhesión intercelular mostraron un patrón de mayor riesgo cardiovascular en las mujeres postmenopáusicas frente a las premenopáusicas. Las moléculas solubles de adhesión vascular parecen influenciadas no sólo por la edad y la menopausia, sino por otros factores como la dieta habitual.

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Palabras clave: Premenopausia. Postmenopausia. Lipemia postprandial. Moléculas de adhesión.

## Introduction

The aging process is associated with several structural and functional metabolic modifications. In turn, these changes may increase the individual's susceptibility to develop conditions such as atherosclerosis, diabetes, obesity, cardiovascular disease and metabolic syndrome.<sup>1</sup>

Due to successive meal intakes, humans spend a large part of the day in a postprandial state. Fat-rich meals result in an increase in triacylglycerolemia and modifications in lipoprotein pattern. The extent and kinetics of such postprandial changes are highly variable and are modulated by numerous factors. Postprandial lipoprotein metabolism is affected by dietary habits, meal composition (amount and type of fat, carbohydrates, proteins, fibre and alcohol), lifestyle practices (physical activity, tobacco use), physiological factors (age, gender, menopausal status) and pathological conditions (obesity, insulin resistance, diabetes mellitus, etc.).<sup>2-4</sup> Abnormalities during the postprandial state contribute to the development of atherosclerosis and cardiovascular risk.<sup>5</sup>

There are very few studies comparing postprandial lipid metabolism before and after menopause.<sup>6-8</sup> Postprandial lipaemia is generally studied with test meals like fat-rich liquids or creams, which do not reflect the texture of common foods and therefore may be digested differently to usual food. We studied postprandial changes in serum triacylglycerol (TAG) and in total cholesterol (Chol) concentrations after a regular fat-rich meal. The fat content was designed to reflect fatty acid composition of the Spanish Mediterranean Diet.<sup>9</sup> The majority of studies have tested the effects of a fat load rich in saturated fatty acids, but the lipid profile exert a marked influence in postprandial lipaemia, and monounsaturated fatty acids induce a lower increase in chylomicron triacylglycerols.<sup>10,11</sup>

Adhesion molecules are markers of endothelial dysfunction and early stages of atherogenesis. Soluble intercellular adhesion molecules (ICAM-1) and vascular adhesion molecules (VCAM-1) are associated with cardiovascular diseases, cancer and autoimmune disorders<sup>12</sup> and have been shown to decrease after dietary treatment.<sup>13</sup>

This study compared endothelial adhesion molecule levels and postprandial lipaemia response to a high monounsaturated meal of healthy postmenopausal (PoW) and young premenopausal (PrW) Spanish women.

## Subjects and methods

### *Study population and study design*

Twenty PrW recruited through flyers distributed throughout the university campus and eighteen PoW recruited from the Menopause Program of the Madrid

City Council of the Food and Health Department participated in the study. This study was conducted in accordance with the ethical rules of the Helsinki Declaration (Seoul, Korea, October 2008). All women gave written informed consent to a protocol approved by the Ethics Committee of the Spanish Council for Scientific Research and the Ethics Committee of the Hospital Clinica Puerta de Hierro. None of the women suffered from any digestive or metabolic disease, as verified by medical history and fasting blood indexes.

For the group of young women, individuals selected had to be healthy, between 18 and 45 years old, premenopausal, not pregnant, not obese (BMI < 30 kg/m<sup>2</sup>), and could not be taking medication known to affect bone and lipid metabolism or be taking vitamin, mineral or phytoestrogen supplements. Women for the postmenopausal group had to be amenorrhic for at least one year, could not be obese (BMI < 30 kg/m<sup>2</sup>), could not be receiving oestrogen replacement therapy or any other medication known to affect bone and lipid metabolism or be taking vitamin, mineral or phytoestrogen supplements. None of the women smoked.

Women visited the laboratory facilities after 12 h overnight fast. In order to unify food intake the evening before the study, all women followed written instructions with regard to dinner composition (lettuce and tomato with olive oil, vinegar and salt; grilled chicken file; bread and fruit). On the morning of the visit blood pressure, weight and height were measured and compliance with dinner instructions was verified with a questionnaire. After baseline venous blood samples were obtained using a cannula (ABOCATH 20G, Abbott Laboratories, Abbott Park, Illinois, USA).

The study meal (Table 1) provided 4552 kJ and contained 75.3 g of fat, 21.5 g of protein, 86.5 g of carbohydrates 2.1 g of fibre and 289 mg of cholesterol. In this meal, proteins, lipids and carbohydrates contributed 7.9%, 62.3%, and 6.6% of total energy, respectively, while 11.8% of the total energy supplied by lipids came from SFA, 39.7% from MUFA and 6.6% derived from PUFA. Postprandial blood samples were taken 60, 120, 240, 360 and 420 min after the end of the study meal. To maintain hydration throughout the postprandial time, women drank 100 ml of demineralised water after 240 min and 390 min after eating. Blood samples were collected in Venoject tubes with Gel + Clot Activator.

### *Measurements*

Blood samples were chilled, then centrifuged for 15 min at 1500 x g and 4°C, and subsequently stored at -80°C. Serum Chol and TAG were determined using automated enzymatic methods (CHOD-PAP and GPO-PAP; Boehringer Mannheim, Germany; RA-XT Technicon, Tarrytown, NY). Soluble serum intercellular adhesion molecules-1 (sICAM-1) and soluble vascular adhesion molecules-1 (sVCAM-1) concentrations

were measured by means of a commercially available ELISA kit (Parameter, R&D Systems).

### Data analysis

Statistical analyses of the results were performed using SPSS 14 for Windows XP. Data are presented as mean and standard deviation. Baseline parameters of anthropometric data, serum lipid and endothelial adhesion molecules were compared with a one-way ANOVA. TAG data were log normalized for statistical analysis. Postprandial TAG were adjusted by subtracting baseline values. Correlation between baseline and postprandial parameters was studied by the Spearman's rank test. Total area under the curve (TAUC) for TAG concentrations was calculated and a one-factor repeated measures ANOVA was performed. A one-factor repeated-measures ANOVA with a between subject-factor group was carried out for serum Chol and TAG for time and time x group interaction. When group x time interaction was significant, one-way ANOVA was used to compare serum Chol and TAG concentrations between groups at each time point. A one-factor repeated-measures ANOVA (time) was performed to determine differences in Chol and TAG concentrations within each group of women and to study peak concentrations of serum Chol and TAG. A Bonferroni post hoc analysis was performed except for time to peak, which was calculated and analysed using the Mann-Whitney test. P values < 0.05 were considered statistically significant.

### Results

All 20 PrW and 18 PoW, completed the study. Subjects of the premenopausal group were between the ages of 18 and 36 and those from the postmenopausal group were between 51 and 59 years of age. Standard meal composition is shown in table I. Anthropometric data, serum lipid and endothelial adhesion molecule values, shown in table II, present significant differ-

<i>Ingredients</i>	<i>Weight</i>
Whole cow's milk (g)	150
Instant coffee (decaffeinated) (g)	2
Avocado (g)	80
Crabsticks (g)	44
Mayonnaise (g)	30
Olive oil (g)	33
Egg (g)	51
Sugar (g)	33
Wheat flour, white (g)	33
White bread, toasted (g)	18
Saccharin (g)	1
Low mineral water (ml)	500

ences between PrW and PoW in all parameters except for sVCAM.

The TAUC of TAG concentration was significantly higher in PoW than in PrW ( $p < 0.0001$ ). There was a significant time effect ( $p < 0.0001$ ) and a significant time x group interaction ( $p < 0.0001$ ) for TAG concentrations (fig. 1). A one-factor (time) repeated-measures ANOVA performed to analyse TAG concentrations in each group of women showed that the significant time effect in both groups was maintained. Differences between time points were more pronounced in PoW than in PrW. Baseline TAG concentrations were significantly lower than those of all other time points in PoW ( $p = 0.001$  compared to 1 h,  $p < 0.0001$  compared to 2 h, 4 h and 6 h, and  $p = 0.02$  compared to 7 h), whereas in PrW, baseline concentrations were only significantly lower than those of the first two time points ( $p < 0.0001$  compared to 1 h and  $p = 0.002$  compared to 2 h) while no significant differences

<i>Parameter</i>	<i>Premenopausal women (n = 20)</i>	<i>Postmenopausal women (n = 18)</i>	<i>ANOVA p</i>
Age (y)	20.9 ± 2.24	55.7 ± 2.4	< 0.0001
Body weight (kg)	58.17 ± 7.34	64.2 ± 6.6	0.012
BMI (kg/m <sup>2</sup> )	21.58 ± 2.25	26.89 ± 3.04	< 0.001
Total serum cholesterol (mg/dL)	171.60 ± 24.37	211.61 ± 27.45	< 0.0001
Serum triacylglycerols (mg/dL)	64.85 ± 30.07	96.83 ± 34.87	0.004
sVCAM (µg/L)	561.05 ± 126.25	522.52 ± 229.53	NS
sICAM (µg/L)	212.88 ± 30.93	311.36 ± 48.40	< 0.0001

\*Data are presented as mean ± SD.

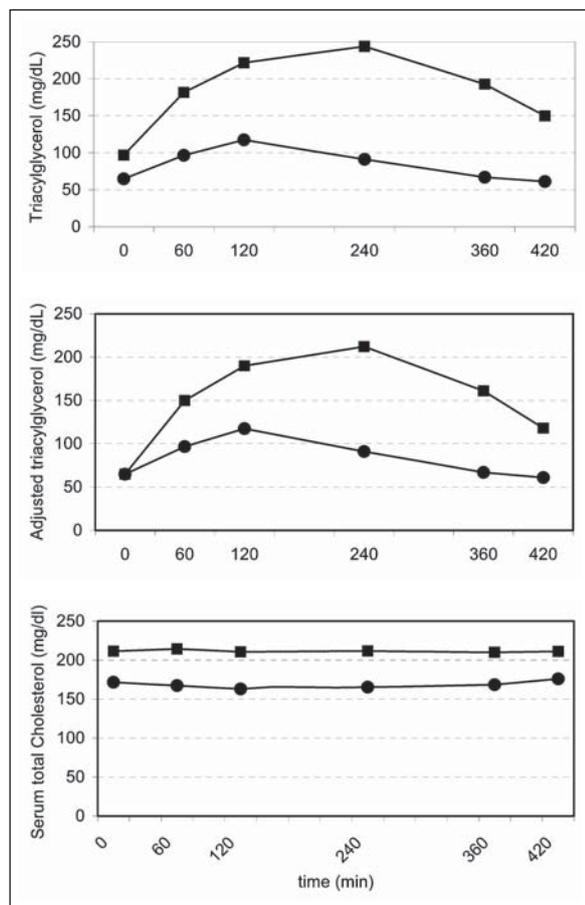


Fig. 1.—Baseline and postprandial serum triacylglycerol and total cholesterol in mg/dL in premenopausal (●) and postmenopausal (■) women after consuming a fat-rich standard area.

between time points 4 h, 6 h, 7 h were observed in PrW. When the postprandial TAG values were adjusted to the baseline data the differences between PrW and PoW remained significant.

Peak concentration and time to peak of serum TAG were significantly higher in PoW than in PrW ( $p = 0.024$  and  $p = 0.038$  respectively) (fig. 1).

In addition, a significant time effect ( $p = 0.001$ ) and time x group interaction ( $p < 0.0001$ ) were observed for total Chol concentrations. When performed a repeated measures one factor (time) ANOVA of Chol concentrations for each group of women total Chol concentrations of PoW showed no time effect. Those of PrW, on the other hand, displayed a significant time effect ( $p < 0.0001$ ), as concentrations after 1 h, 2 h and 4 h in these females were significantly lower than those obtained after 7 hours ( $p < 0.043$ ,  $p = 0.003$  and  $p = 0.005$ , respectively), while no significant differences were observed between baseline, 6 h and 7 h values (fig. 1).

## Discussion

This study clearly shows that PoW display higher postprandial lipaemia than PrW in response to a fat-

rich standard meal, and the TAG concentration in PoW is delayed without returning to baseline levels. Even when adjusting for TAG baseline values, these differences were still observed.

To our knowledge this is the first study that compares premenopausal and postmenopausal postprandial response to a meal containing foods with a lipid profile similar to that of the Mediterranean diet. Postprandial lipaemia is influenced by various parameters such as gastric emptying time, intestinal absorption and lipoprotein lipase activity.<sup>6</sup> With age, gastric emptying rate and lipoprotein lipase activity are known to decrease, and a reduction of pancreatic lipase secretion and a delay in the clearance of TAG-rich lipoproteins have also been observed.<sup>6</sup> Bibliographical data on postprandial metabolism in pre and postmenopausal women are scarce and the studies that have been undertaken involve very small numbers of subjects. It is also difficult to compare data due to the variety of food employed in the different studies. The lower postprandial lipaemia displayed by the PrW in the present study was also found in other studies, with levels of TAG for post- and PrW similar to our data, although in average our PrW were younger.<sup>14</sup> Nabeno et al.<sup>6</sup> reported similar results, but differ in the baseline characteristics of the women studied and in the food consumed, which was given as a fat-rich cream.

Chol levels in the postmenopausal group did not vary during digestion, while in the young PrW Chol levels clearly decreased. Other authors described stable postprandial Chol levels in healthy young men and women.<sup>15-17</sup> Cohn et al.<sup>8</sup> reported that postprandial plasma Chol concentrations can increase, decrease, or remain essentially unchanged, while Nabeno et al.<sup>6</sup> observed that Chol values tended to decrease, although not significantly, during the first hours in young premenopausal women, but not in older premenopausal female which is in agreement with the present results. We found significantly higher fasting HDL-cholesterol levels in PrW than in PoW. In this regard, high fasting baseline HDL-Chol levels relate with lower postprandial lipaemia.<sup>8</sup>

Comparing endothelial function between these women, unexpectedly we observed no differences in the sVCAM-1 concentrations, but sICAM-1 levels were lower in PrW than in PoW. Reports<sup>18,19</sup> indicate that sICAM levels predict better CVD and diabetes risk in healthy subjects and patients. In our healthy PrW and PoW we did not find any association between sICAM-1 levels and fasting insulin concentration (data not shown) which is in accordance with the results obtained by Blüher et al.<sup>20</sup> who found no correlation between these adhesion molecules and fasting insulin and glucose neither in control subjects nor in patients with impaired glucose tolerance or Type II diabetes. Also some authors report a negative correlation between estradiol concentration and sICAM levels,<sup>21,22</sup> which is consistent with these data, presenting PrW lower levels of sICAM than the PoW. We previously observed that postmenopausal women exhibited higher CVD risk and insulin resistance compared with premenopausal young women.<sup>23,24</sup>

Richter et al.<sup>25</sup> compared sVCAM and sICAM values of Dutch vegetarians and non-vegetarians of different ages. These authors state that sICAM levels are influenced by age but not diet. Contrary in sVCAM levels, in older vegetarians they found lower sVCAM levels than those of non-vegetarians of the same age. The PoW of this study consumed a habitual diet, which closely conforms to current nutritional guidelines, eating high quantities of fruits, vegetables and fish and little meat, sugar, sweets and pastry,<sup>26</sup> whereas PrW of this study showed a less favourable dietary intake with lower fruit and vegetables, and higher meat and pastry intake.<sup>27</sup> In this line low sVCAM-1 levels in these PoW could be related to their high antioxidant and fibre intake.

However, the influence of age on adhesion molecules remains controversial. Several authors discuss the influence of age on sICAM and sVCAM levels<sup>25,28-31</sup> of men and women of different age groups, and rats. Future research regarding the normative data of adhesion molecules in men and women of different ages and on the relations between these biomarkers and risk of chronic diseases, including cardiovascular, diabetes and autoimmune disorders, as well as the influence of diet, are needed.

## Conclusion

Postprandial lipaemia after consuming a meal with lipid profile similar to that of the Mediterranean diet show a higher cardiovascular risk pattern in postmenopausal compared to premenopausal women. Intercellular adhesion molecule concentrations also show a higher cardiovascular risk in the postmenopausal women. However, vascular adhesion molecules seem to be influenced not only by age and menopause, but also other factors like usual diet, which was less balanced in the young women.

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