Epidemiology and Prevention

Effect of the Mediterranean Diet on Fasting Concentrations of Activated Factor VII in Healthy Persons

Introduction and objectives. Many clinical and epidemiologic studies suggest that activated factor VII may be involved in the pathogenesis of coronary heart disease. Our objective was to determine the effect of a Mediterranean diet on plasma levels of activated factor VII in comparison to a low-fat diet and a diet rich in saturated fat.

Patients and method. The study population comprised 16 healthy normolipemic men who consumed 3 different diets in consecutive 28-day periods. The first diet was rich in saturated fat (38% calories as fat, 20% saturated fat), the second was a low-fat, high-carbohydrate diet (28% calories as fat, 10% saturated fat), and the third was enriched in monounsaturated fatty acids (38% calories as fat, 22% monounsaturated fat). At the end of each period, plasma concentrations of total cholesterol, HDL cholesterol, LDL cholesterol, total triglycerides, apolipoprotein A-I, apolipoprotein B, and glucose were measured. Activated factor VII was determined with a coagulation assay.

Results. The diet rich in saturated fat was associated with a significant increase in total cholesterol, LDL cholesterol, apolipoprotein AI, and apolipoprotein B in comparison to the other 2 diets. There were no significant differences between the carbohydrate-rich diet and the Mediterranean diet in any of the lipid parameters. The Mediterranean diet decreased plasma levels of factor VIIa in comparison to the diet rich in saturated fat (34.6±15.3 mU/mL vs 101.5±19.2 mU/mL; P<0.05).

Conclusions. In comparison to the diet rich in saturated fat or the high-carbohydrate diet, the Mediterranean diet decreased plasma concentrations of activated factor VII in healthy young men. This phenomenon may constitute another protective mechanism of the Mediterranean diet in reducing cardiovascular risk.

Key words: Mediterranean diet. Activated factor VII. Cardiovascular risk.


Efecto de la dieta mediterránea en los valores plasmáticos de factor VII activado en personas sanas

Introducción y objetivos. Numerosos estudios clínicos y epidemiológicos sugieren que el factor VII activado puede estar implicado en la patogenia de la enfermedad coronaria. Nuestro objetivo es determinar el efecto de una dieta típica mediterránea en los valores plasmáticos de dicho parámetro, cuando se compara con una dieta pobre en grasa y con una dieta rica en grasa saturada.

Pacientes y métodos. Dieciséis varones sanos normolípidicos recibieron 3 dietas, durante 4 semanas cada una. La primera era rica en grasa saturada (38% grasa, 20% saturada), la segunda rica en hidratos de carbono y pobre en grasa (28% grasa, 10% saturada) y, finalmente, una dieta mediterránea (38% grasa, 22% de grasa monounsaturada). Al final de cada período se determinaron las concentraciones plasmáticas de colesterol total, colesterol HDL, LDL, triglicéridos, apolipoproteína A-I, apolipoproteína B, y glucosa. El factor VII activado se midió mediante un ensayo de coagulación.

Resultados. La dieta rica en grasa saturada se asoció con un incremento significativo de los valores de colesterol total, cLDL, apolipoproteína A-I y apolipoproteína B, en comparación con las otras 2 dietas. No hubo diferencias significativas entre la dieta rica en hidratos de carbono y la mediterránea para cualquiera de los parámetros lipídicos examinados. El paso de una dieta rica en grasa saturada a una dieta mediterránea produjo un descenso en los valores de FVIIa (101.5±19.2 frente a 34.6±15.3 mU/mL; p<0.05).

Conclusiones. La dieta mediterránea, cuando se compara con la dieta rica en grasa saturada o la rica en hidratos de carbono, disminuye las concentraciones plasmáticas del factor VII activado en varones sanos. Este fenómeno podría constituir otro mecanismo protector de la dieta mediterránea en la reducción del riesgo cardiovascular.

INTRODUCTION

Factor VII (FVII) is a vitamin K-dependent plasma glycoprotein which has an important role in initiating the tissue-factor induced coagulation cascade (the extrinsic pathway of blood clotting). Several clinical studies have suggested that factor VII clotting (FVIIc) activity in middle-aged persons is directly associated with the risk for cardiovascular disease. Moreover, the values of activated factor VII (FVIIa) are also related with cardiovascular risk, independently of other factors, such as systolic blood pressure, triglycerides, obesity, or levels of apolipoprotein A-I. Thus, FVII may have an important role in the pathogenesis of arteriosclerosis.

Although several different techniques are available to measure FVII, they are not all comparable, which may explain the inconsistent results of different studies. The most commonly used assay is FVIIc, which measures total concentrations of both FVIIc and FVIIa. Since the function of the activated form is to initiate the coagulation chain, measurement of FVIIa would appear to be the most interesting method of studying FVII. To date, specific assays to measure FVIIa in plasma, which is a better predictor of risk than either FVII or FVIIc, have shown that healthy subjects have significantly low levels.

Recent dietary intervention studies have shown that various plasma components related to the thrombotic process may be affected by the fatty acid composition of the diet. An example is the demonstration that a diet enriched in saturated fatty acids raises plasma levels of FVII and induces activation of FVIIc during the post-prandial period. Earlier studies have shown that diets poor in fats and rich in carbohydrates have a reduced effect on FVIIc. However, the influence of this type of diet on FVIIa has not yet been studied. Accordingly, we examined the effects on FVIIa concentrations of 3 types of diet: a diet rich in saturated fats, a diet rich in carbohydrates, and a Mediterranean diet.

PATIENTS AND METHODS

Study Population and Diets

The study population comprised 16 healthy normolipidemic men from the University of Cordoba. Prior to the study, a clinical history was taken and a laboratory analysis was performed for the participants, all of whom were younger than 30 years of age (mean age, 20.8±2.1), had plasma concentrations of total cholesterol <5.2 mmol/L, no evidence of any chronic liver, kidney, heart or thyroid disorder, and none of them had a regularly high level of physical exercise. The participants had no family history of cardiovascular disease and had not taken any medication or dietary or vitamin supplements for 6 months prior to the study. The dietary information, which included alcohol consumption, was collected for 7 consecutive days. The individual energy requirements were calculated taking into consideration each person’s physical activity. The participants were encouraged to continue their usual lifestyle and level of physical exercise and were asked to write down in a diary any event which might alter this pattern, such as stress, changes in smoking habits, and the consumption of alcohol or meals not included in the experimental design.

All the participants consumed 3 different diets over consecutive 28-day periods. In order to maintain a stable weight, the diets were isocaloric in relation to the participants’ previous usual energy intake. The first diet consisted of a stabilization diet rich in saturated fat (SAT diet), containing 15% of the energy in the form of proteins, 47% as carbohydrates and 38% as fat (20% saturated fat, 12% monounsaturated fat, and 6% polyunsaturated fat). The second diet was rich in carbohydrates (CH diet) and consisted of 15% proteins, 57% carbohydrates, and 28% fat (<10% saturated fat, 12% monounsaturated fat, and 6% polyunsaturated fat). Finally, the third diet was a Mediterranean diet (MED diet), which was rich in olive oil, with 15% proteins, 47% carbohydrates, and 38% total fat (10% saturated fat, 22% monounsaturated fat, and 6% polyunsaturated fat). There was no washout period between diets. The mean intake of cholesterol during the 3 dietary periods was 115 mg/1000 kilocalories. The study was approved by the Clinical Research Ethics Committee of the Hospital Universitario Reina Sofia, Cordoba, Spain.

The composition of the experimental diets was calculated from the food tables of the United States Department of Agriculture (USDA) or the Spanish food composition tables corresponding to local foods. The experimental design of the study involved 20 previously established rotating menus, each of which used natural foods calibrated to provide the established proportions for each of the dietary periods. The monounsaturated fat in the Mediterranean diet was derived from the virgin olive oil used to cook the meals, dress the salads and put on toast. Lunch and dinner were always provided by and eaten in the dining room of the Hospital Universitario Reina Sofia, under supervision by us and a team dietician. Breakfast and tea were served according to our instructions in the cafete-
Tungstic acid. LDL cholesterol was calculated by precipitation with phospho-
lipids were considered significant if the
Wilcoxon test (which corresponds to paired data). Vari-
ween the 3 diets did not follow a normal distribution
analysis was undertaken with the Tukey test to iden-
tify differences between the groups. Because the
differences were significant, a post hoc analysis was undertaken with the Tukey test to identify differences between the groups. Because the differences in the plasma concentrations of FVIIa bet-
 tween the 3 diets did not follow a normal distribution they were analyzed by Friedman ANOVA and the Wilcoxon test (which corresponds to paired data). Values were considered significant if the P was less than .05. Data are presented as the mean ± standard deviation (SD).

RESULTS

Table 1 shows the age, the body mass index, and the baseline values of plasma lipids and apolipoprotein levels in the study subjects. The dietary composition was analyzed in duplicate portions of meals and was in agreement with that given in the corresponding food composition tables (Table 2). The plasma concentra-
tions of lipids and apolipoproteins at the end of each dietary intervention period are shown in Table 3. The SAT diet had higher levels of total cholesterol, LDL cholesterol, apolipoprotein A-1, and apolipoprotein B than the CH diet (P<.05) and the MED diet (P<.001). No significant differences were detected for any of the lipid parameters studied between the CH and the MED diets. Consumption of the MED diet was associated with a significant reduction in plasma concentrations of FVIIa in comparison with the CH diet (P<.05) and the SAT diet (P<.05) (Table 3).

DISCUSSION

The results of this study showed that eating a Medi-
terranean type diet, rich in olive oil, lowered the levels of FVIIa in a group of healthy volunteers, in compar-
sion with a diet rich in saturated fatty acids and another rich in carbohydrates. There was a positive correlation between the reduction in FVIIa levels and the concen-

TABLE 1. Baseline Characteristics (Mean ±SD) of the Men (n=16) Who Participated in the Study

<table>
<thead>
<tr>
<th></th>
<th>Age, years</th>
<th>BMI</th>
<th>Triglycerides, mmol/L</th>
<th>Total cholesterol, mmol/L</th>
<th>HDL cholesterol, mmol/L</th>
<th>LDL cholesterol, mmol/L</th>
<th>Apo A-1, g/L</th>
<th>Apo B, g/L</th>
</tr>
</thead>
<tbody>
<tr>
<td>SAT Diet</td>
<td>20.8±2.1</td>
<td>23.6±1.9</td>
<td>0.9±0.4</td>
<td>3.9±0.6</td>
<td>1.2±0.3</td>
<td>2.3±0.6</td>
<td>1.10±0.2</td>
<td>0.56±0.1</td>
</tr>
<tr>
<td>CH Diet</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MED Diet</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Apo indicates apolipoprotein; BMI, body mass index.

TABLE 2. Daily Mean Intake (mean ±SD) During the 3 Dietary Intervention Periods

<table>
<thead>
<tr>
<th></th>
<th>SAT Diet</th>
<th>CH Diet</th>
<th>MED Diet</th>
</tr>
</thead>
<tbody>
<tr>
<td>Protein, % energy</td>
<td>17.9±2.5</td>
<td>17.3±1.5</td>
<td>17.5±2.0</td>
</tr>
<tr>
<td>Fat, % energy</td>
<td>38.1±2.9</td>
<td>28.1±2.8</td>
<td>38.6±3.5</td>
</tr>
<tr>
<td>Saturated</td>
<td>23.1±4.1</td>
<td>9.0±3.5</td>
<td>9.1±4.2</td>
</tr>
<tr>
<td>Monounsaturated</td>
<td>10.0±2.9</td>
<td>13.12±2.2</td>
<td>24.7±2.3</td>
</tr>
<tr>
<td>Polyunsaturated</td>
<td>5.0±1.5</td>
<td>6.0±2.4</td>
<td>4.8±1.1</td>
</tr>
<tr>
<td>Carbohydrates, % energy</td>
<td>44.0±8.3</td>
<td>54.6±8.6</td>
<td>43.9±7.8</td>
</tr>
<tr>
<td>Cholesterol, mg/1000 kcal</td>
<td>112±39</td>
<td>114±48</td>
<td>115±42</td>
</tr>
<tr>
<td>Energy, MJ</td>
<td>10.2±1.1</td>
<td>10.3±1.0</td>
<td>10.5±1.5</td>
</tr>
</tbody>
</table>

*CH indicates carbohydrate-rich diet; MED, diet rich in monounsaturated fats; SAT, diet rich in saturated fats.
TABLE 3. Plasma Concentrations of Lipids and Apolipoproteins (mmol/L) at the End of Each Dietary Intervention Period

<table>
<thead>
<tr>
<th></th>
<th>SAT diet</th>
<th>CH diet</th>
<th>MED diet</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cholesterol, mmol/L</td>
<td>4.35±0.61†‡</td>
<td>3.62±0.4</td>
<td>3.79±0.5</td>
</tr>
<tr>
<td>Triglycerides, mmol/L</td>
<td>0.91±0.3</td>
<td>0.85±0.4</td>
<td>0.80±0.3</td>
</tr>
<tr>
<td>HDL cholesterol, mmol/L</td>
<td>1.60±0.2</td>
<td>1.16±0.3</td>
<td>1.24±0.3</td>
</tr>
<tr>
<td>LDL cholesterol, mmol/L</td>
<td>2.67±0.51‡</td>
<td>2.06±0.4</td>
<td>2.18±0.5</td>
</tr>
<tr>
<td>Apo A-1, g/L</td>
<td>1.20±0.11‡</td>
<td>1.08±0.2</td>
<td>1.12±0.2</td>
</tr>
<tr>
<td>Apo B, g/L</td>
<td>0.58±0.11†‡</td>
<td>0.46±0.1</td>
<td>0.50±0.1</td>
</tr>
<tr>
<td>FVIIa, mU/mL</td>
<td>101.5±19.2</td>
<td>67.8±11.5</td>
<td>34.6±15.3†‡</td>
</tr>
</tbody>
</table>

*Applies to apolipoprotein: CH, carbohydrate-rich diet; BMI, body mass index; MED, diet rich in monounsaturated fats; SAT, diet rich in saturated fats.
†Significantly different from the CH diet (P<.004).
‡Significantly different from the SAT diet (P<.0004).
§Significantly different from the SAT diet (P<.002).

![Text](https://www.revespcardiol.org/)

ACKNOWLEDGEMENTS

The authors thank Marino Uceda and Antonio Jiménez for their technical help in the measurement of the fatty acid composition of cholesterol esters in the LDL and Rosario López for her technical help with the measurement of plasma concentrations of FVIIa.

REFERENCES


2. Meade TW, Mellows S, Brozovic M, Miller GJ, Chakrabarti RR,


