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Fernando Cardona, Francisco Jose Tinahones, Eduardo Collantes, Alejandro Escudero, Eduardo Garcia-fuentes, and Federico Soriguer

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CONTRIBUTION OF POLYMORPHISMS IN THE APOLIPOPROTEIN AI-CIII-AIV CLUSTER TO HYPERLIPIDEMIA IN PATIENTS WITH GOUT

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ABSTRACT

Studies have shown that hyperuricemia is independently related with the insulin resistance syndrome and that polymorphisms of the apolipoprotein AI-CIII-AIV cluster are related with insulin resistance. We studied the prevalence of polymorphisms of the apolipoprotein AI-CIII-AIV cluster in persons with gout and determined whether these polymorphisms contribute to its pathophysiology or to altered lipid levels. Plasma levels of cholesterol, triglycerides, uric acid, VLDL, LDL, IDL and HDL triglycerides and cholesterol, plus renal excretion of uric acid were studied in 68 patients with gout and 165 healthy subjects. Polymorphisms were studied by amplification and RFLP in all subjects using XmnI and MspI in the apolipoprotein AI gene and SstI in the apolipoprotein CIII gene. The A allele at position -75 bp in the apolipoprotein AI gene was more common in patients with gout than in controls (p=0.01). Levels of cholesterol, triglycerides, uric acid, basal glycemia and HDL cholesterol were higher in the patients (p<0.001). The patients also presented an interaction between mutations at the two polymorphic loci studied in the apolipoprotein AI gene (p=0.04); an absence of the mutation at position -75 bp of the apolipoprotein AI gene resulted in increased plasma triglyceride levels. Gouty patients thus have a different allelic distribution in the apolipoprotein AI-CIII-AIV cluster, which could lead to changes in levels of lipoproteins. However, this is not caused by a single mutation but rather a combination of the different mutations.

Key Words: apolipoprotein AI-CIII-AIV cluster, gout, polymorphisms, Hyperuricemic.
INTRODUCTION

Hyperuricemia appears to be an independent risk factor for coronary heart disease (1-3). Although the reason for this is not well known, evidence suggests that hyperuricemia forms part of the metabolic syndrome. A high concentration of uric acid is closely related with hyperinsulinemia, glucose intolerance, hypertension, dyslipidemia, very high levels of triglycerides, low levels of HDL cholesterol, obesity and especially abdominal adiposity (4-12). Regarding the association, already demonstrated, between hyperuricemia and hyperlipidemia, we have previously shown the existence of two groups of hyperuricemic patients, those in whom the hyperuricemia is associated with hyperlipidemia who could be considered to have the metabolic syndrome and those having no association with any metabolic disorder (13). We have also reported that hyperuricemic-hypertriglyceridemic patients have high levels of VLDL components and a reduced fractionated excretion of uric acid and an increased ratio of CIII to CII apolipoproteins. Apolipoproteins therefore play an important role in the pathophysiology of the changes seen in hyperuricemia (14).

Apolipoproteins AI-CIII-AIV are lipid binding proteins, that are involved in the transport of lipids in plasma. Defects or variations in these apolipoproteins are also associated with altered levels of lipids and lipoproteins. The relationship between variations in the apolipoprotein AI-CIII-AIV gene cluster and plasma lipid features has long been recognised. Most studies have concentrated on the association between plasma triglycerides and variations in the gene cluster (15). Upregulation of apolipoprotein CIII in transgenic mice induces hypertriglyceridemia because this apoprotein is involved in VLDL clearance (16). The apoprotein CIII gene is closely linked with the apolipoprotein AI and AIV genes on chromosome 11, forming a cluster. Study of polymorphisms in this cluster has shown that the S2 allele of the polymorphism is related with hypertriglyceridemia and an increased risk for coronary heart disease (17-18). López-Miranda et al. showed that carriers of the S2 allele have reduced concentrations of LDL cholesterol when given a diet rich in monounsaturated fats (19). Furthermore, the change of a G for an A at position -75 bp in the promoter region of the apolipoprotein AI gene, digested by the restriction enzyme MspI, induces increased transcription of this gene and increased serum levels of apolipoprotein AI (20). Persons with this mutation also have higher levels of HDL cholesterol. Although not yet demonstrated, it would appear that this can be explained by linkage disequilibrium between the A allele and another functional mutation in the gene. Another mutation exists in the 5’ region, near the apolipoprotein AI gene -2500 bp upstream from the restriction start site which is the marker for combined family hyperlipidemia or hypertriglyceridemia (21-23). These data show that the cluster of apolipoprotein AI-CIII-AIV genes is involved in hypertriglyceridemia, and may also be involved in predisposition to atherosclerosis.

We studied the prevalence of polymorphisms of the apolipoprotein AI-CIII-AIV cluster in persons with gout and determined whether these polymorphisms contribute to the pathophysiology of hyperuricemia or to altered lipid levels in these persons.
MATERIAL AND METHODS

Subjects

The study was undertaken in 68 men with gouty from the Rheumatology Service at the Hospital Reina Sofía in Cordoba, Spain. None were receiving lipid lowering or urate-lowering therapy. Height and weight were also measured and the body mass index (BMI) calculated.

Patients with secondary hyperuricemia (renal failure or use of diuretics) were excluded from the study. A control group was composed of 165 healthy persons with no history of gout, with cholesterol and triglyceride levels lower than 200 mg/dl, selected from a local cross-sectional study (24) and adjusted for age.

Procedures

DNA analysis

DNA was isolated from venous blood by the "salting out" method of Miller (25), modified by Queipo-Ortuño (26), and amplified by polymerase chain reaction in a thermocycler (mastercycler Eppendorff). Primers for the XmnI locus (at position -2500 bp upstream of the transcription start site of the apolipoproteins A1) were those described by Shoulders et al. (27), for the -75 bp locus of the apolipoprotein A1 gene (determined by MspI) those of Jeenah et al. (28) and for the SstI locus of the apolipoprotein CIII gene those of Dammerman et al. (29).

Laboratory Analysis

Venous blood samples, collected after a 12-hour fast, were ultracentrifuged at 2000g x 15 minutes for measurement of lipids and lipoproteins. Plasma levels of glucose, cholesterol, triglycerides, creatinine, HDL cholesterol, LDL cholesterol and uric acid were measured in an autoanalyzer using calorimetric assays (Ecoline 25, Diagnostica Merck). Calculations were made of uric acid clearance and the 24-hour uric acid urinary excretory fraction.

Lipoproteins were separated from serum by ultracentrifugation as follows: first, the VLDL fraction was separated from the serum by flotation at 55000 rpm for 18 hours at 7°C in a 45° rotor (Beckman TLA 100.3). After separation of the VLDL, the density of the infranatant was adjusted to 1.30 g/ml by direct addition of potassium bromide and saccharose, separating the rest of the lipoproteins by density gradient centrifugation at 45000 rpm for 22 hours at 7°C in a swinging bucket rotor (Beckman SW 40Ti). To visualize the position of the lipoprotein bands a small amount (25µl) of saturated Coomassie blue was added. The concentrations of cholesterol and triglycerides were measured in each fraction as above. The amount of HDL cholesterol was also measured by the alternative method of precipitation with phosphotungstic acid in patients and controls. The LDL cholesterol was calculated from the Friedewald equation.
Statistical Analysis

Data are expressed as the mean ± standard deviation (SD). Comparison between groups was made with Student’s $t$ test for independent variables and Mann-Whitney $U$ test according to the normality of the variables. Differences in the genotype distribution of the apolipoprotein AI-CIII-AIV cluster were studied by $\chi^2$ square test. Statistical analyses were performed with SPSS 6.0 for Windows and $P$ values < 0.05 were considered significant.
RESULTS

The clinical and laboratory data for the patients and controls are summarized in Table 1. Plasma levels of cholesterol, triglycerides and uric acid were greater in patients with gout than the controls (211.7±40.3 vs. 173.2±17.3; 246.5±222.0 vs. 89.3±40.0; 7.7±1.7 vs 5.2±1.2 mg/dL, respectively; p<0.001). The patients also had higher plasma HDL cholesterol levels (47.1±12.4 vs. 41.8±9.1 mg/dL; p<0.001) and a higher BMI (30.2±3.8 vs. 27.3±3.7; p<0.001) than the controls (Table 1).

Frequency Distribution of the Polymorphisms of the Apolipoprotein AI-CIII-AIV Cluster

The frequency of the A allele, i.e. the presence of the mutation in both homozygotes and heterozygotes, was higher in patients than controls (p=0.01). The distribution of the different genotypes of this polymorphism is shown in Table 2. The unusual alleles in homozygotes located -2500 bp upstream of the transcription start site of the apolipoprotein AI gene (determined by XmnI) and of exon 4 of the apolipoprotein CIII gene (determined by SstI) were also more frequent in patients than controls, though the difference was not statistically significant.

Influence of the Polymorphisms of the Apolipoprotein AI-CIII-AIV Cluster on Biological Variables

The effect of these polymorphisms on the study variables differed. The presence of the X2 allele in the controls was not related with any increase in the variables studied, whereas its presence in the patients was related with increased plasma levels of triglycerides (204.5±149.0 vs. 338.0±333.0 mg/dL; p=0.03) (Table 3). The other polymorphisms studied in the apolipoprotein AI-CIII-AIV cluster were not significantly related with any differences in the distribution of the study variables (data not shown).

The content of VLDL triglycerides was greater in those patients with the X2 allele than the non-carriers, adjusted for age and BMI (156.4±173.7 vs. 92.7±62.6 mg/dL; p=0.05) (Table 3). The levels of IDL and LDL triglycerides were also higher in carriers of the mutated allele, though the difference was not statistically significant. There were no significant differences in any of the other lipoprotein fractions studied (Table 3), or in the distribution of the biological variables in either of the other two polymorphisms of the apolipoprotein AI and CIII cluster (data not shown).

The combined distribution of the polymorphisms of the apolipoprotein AI-CIII-AIV cluster was different between the patients and the controls; 63.5% of the patients had some mutation at the two polymorphic sites of the apolipoprotein AI gene studied compared with 41.7% of the controls (p=0.007) (Table 4). The presence of at least one unusual allele was related with significant differences in the lipid content of the lipoprotein fractions (Table 5). VLDL cholesterol was higher in patients with at least one mutation in any of the polymorphisms of the cluster compared to patients with no mutation (p=0.044). The triglyceride content was greater in carriers of some mutation in the cluster than in persons
with no mutation (p=0.014). The IDL cholesterol was higher in carriers of some mutation than non-carriers (p=0.021). HDL cholesterol was also higher in carriers, but the difference was not significant.

DISCUSSION

Hyperuricemia is a risk factor for coronary heart disease (30). The relation between hyperuricemia-hyperlipidemia and renal excretion of urates is known; patients with hyperuricemia-hyperlipidemia have a reduced renal excretion of urates compared with those who just have isolated hyperuricemia; indeed, these latter have also been reported to have low renal excretion of urates (31,2). Besides increased VLDL in these patients, those with hyperuricemia also show a close relation between VLDL levels and renal excretion of urates (32,33). This relation appears to be mediated by the high prevalence of the E2 isoform of apolipoprotein E (34).

Recent studies have related polymorphisms of the cluster with variations in plasma lipid levels. Variations in these genes contribute to combined family hyperlipidemia, modifying plasma concentrations of cholesterol and triglycerides, as well as concentrations of apolipoprotein B and apolipoprotein CIII (35).

Patients with gout have a greater prevalence of mutated genotypes at polymorphic sites of the apolipoprotein AI gene; 18.8% had AA at position -75 bp from the transcription start site versus 6.7% in controls (p=0.01). This high prevalence may be responsible for the high levels of HDL cholesterol seen in patients with gout, as has been described for other disease groups (36, 37, 38, 39).

We also found a greater frequency of the mutated allele at position -2500 bp in the apolipoprotein AI gene, although the difference was not significant. We showed that 63.5% of persons with gout have some mutation at the two polymorphic sites of the apolipoprotein AI gene versus 36.7% who do not have these alleles (p=0.007). These patients with a mutated allele at position -2500bp upstream of the apolipoprotein AI gene had higher plasma and VLDL triglyceride levels than those without the mutation (p=0.05), corrected for BMI; in fact patients with the mutation had a lower BMI than those without the mutation. This allele has been associated with hypertriglyceridemia in patients with combined family hyperlipidemia (40,41). In our group of patients there seems to be a synergic effect of the two polymorphic sites in the influence on plasma triglyceride levels. Patients with gout who had some mutation at the three polymorphic sites studied had higher contents of VLDL, IDL and HDL cholesterol and VLDL triglycerides. Thus, their metabolism of lipoproteins seems to be altered, thereby contributing to the expression of hypertriglyceridemia in these patients. The lipoprotein phenotype characteristic of the insulin resistance syndrome was more prevalent in the gouty subjects with a mutation in the cluster despite their BMI being no greater than subjects without the mutation.

We can conclude that the high prevalence of mutations in the apolipoprotein AI-CIII-AIV cluster in patients with gout partly explains their lipoprotein phenotype and that, jointly, these mutations exert more influence on the polymorphic sites of the apolipoprotein AI gene than the apolipoprotein CIII gene.
Acknowledgments

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REFERENCES


14. Tinahones,-F-J; Collantes,-E; C-Soriguer,-F-J; Gonzalez-Ruiz,-A; Pineda,-M; Anon,-J; Sanchez-Gujo,-P. Increased VLDL levels and diminished renal excretion of uric acid in hyperuricaemic-hypertriglyceridaemic patients. *Br-J Rheumatol.* 1995 Oct; 34(10): 920-4.


### Table 1
Means ± SD of the biological variables in controls and patients with gout

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>Hyperuricemic patients</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>165</td>
<td>68</td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>49.0±10.0</td>
<td>50.0±10.8</td>
<td>0.59</td>
</tr>
<tr>
<td>Glycemia (mg/dL)</td>
<td>103.0±24.6</td>
<td>108.3±19.3</td>
<td>0.18</td>
</tr>
<tr>
<td>Cholesterol (mg/dL)</td>
<td>173.2±17.3</td>
<td>211.7±40.3</td>
<td>0.001*</td>
</tr>
<tr>
<td>Triglycerides (mg/dL)</td>
<td>89.3±40.0</td>
<td>246.5±222.0</td>
<td>0.001*</td>
</tr>
<tr>
<td>HDL chol (mg/dL)</td>
<td>41.8±9.1</td>
<td>47.1±12.4</td>
<td>0.01*</td>
</tr>
<tr>
<td>Uric acid (mg/dL)</td>
<td>5.20±1.2</td>
<td>7.7±1.7</td>
<td>0.001</td>
</tr>
<tr>
<td>LDL chol (mg/dL)</td>
<td>113.5±16.6</td>
<td>120.2±33.9</td>
<td>0.17</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>27.3±3.8</td>
<td>30.2±3.8</td>
<td>0.001*</td>
</tr>
</tbody>
</table>

* p<0.001; after adjustment for age
Table 2

Genotype distribution (%) of the polymorphisms of the cluster in controls and patients with gout

<table>
<thead>
<tr>
<th>Apo AI</th>
<th>Controls</th>
<th>Patients</th>
<th>Apo AI</th>
<th>Controls</th>
<th>Patients</th>
<th>Apo CIII</th>
<th>Controls</th>
<th>Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>165</td>
<td>64</td>
<td>n</td>
<td>165</td>
<td>64</td>
<td>n</td>
<td>165</td>
<td>64</td>
</tr>
<tr>
<td>GG</td>
<td>66.1</td>
<td>51.6</td>
<td>X1X1</td>
<td>79.2</td>
<td>70.3</td>
<td>S1S1</td>
<td>78.8</td>
<td>86.7</td>
</tr>
<tr>
<td>GA</td>
<td>27.3</td>
<td>29.7</td>
<td>X1X2</td>
<td>18.3</td>
<td>25.0</td>
<td>S1S2</td>
<td>20.7</td>
<td>11.7</td>
</tr>
<tr>
<td>AA</td>
<td>6.7</td>
<td>18.8a</td>
<td>X2X2</td>
<td>2.5</td>
<td>4.7</td>
<td>S2S2</td>
<td>0.5</td>
<td>1.7</td>
</tr>
</tbody>
</table>

*a p = 0.01
Table 3

Means ± SD of the biological variables in patients with gout according to the presence or absence of the mutated allele (determined by XmnI) of the polymorphism of the apolipoprotein AI gene

<table>
<thead>
<tr>
<th>Hyperuricemic patients</th>
<th>X1X1</th>
<th>X1X2 / X2X2</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>44</td>
<td>19</td>
</tr>
<tr>
<td>Glycemia (mg/dL)</td>
<td>108.3±22.0</td>
<td>106.0±12.6</td>
</tr>
<tr>
<td>HDL cholesterol (mg/dL) *</td>
<td>34.2±8.4</td>
<td>35.5±9.2</td>
</tr>
<tr>
<td>Uric acid (mg/dL)</td>
<td>7.6±1.7</td>
<td>8.0±1.6</td>
</tr>
<tr>
<td>LDL cholesterol (mg/dL) **</td>
<td>86.9±23.0</td>
<td>87.3±40.0</td>
</tr>
<tr>
<td>Cholesterol (mg/dL)</td>
<td>207.0±38.0</td>
<td>219.0±45.0</td>
</tr>
<tr>
<td>Triglycerides (mg/dL)</td>
<td>204.5±149.0</td>
<td>338.0±333.0</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>28.0±8.5</td>
<td>27.6±8.0</td>
</tr>
<tr>
<td>VLDL cholesterol (mg/dL)</td>
<td>19.2±12.9</td>
<td>26.1±15.3</td>
</tr>
<tr>
<td>VLDL triglycerides (mg/dL)</td>
<td>92.7±62.6</td>
<td>156.5±173.7</td>
</tr>
<tr>
<td>LDL cholesterol (mg/dL)</td>
<td>118.6±30.2</td>
<td>127.9±44.8</td>
</tr>
<tr>
<td>LDL triglycerides (mg/dL)</td>
<td>54.2±55.9</td>
<td>71.4±87.1</td>
</tr>
<tr>
<td>IDL cholesterol (mg/dL)</td>
<td>15.1±11.0</td>
<td>15.3±10.3</td>
</tr>
<tr>
<td>IDL triglycerides (mg/dL)</td>
<td>21.9±18.3</td>
<td>29.2±28.5</td>
</tr>
<tr>
<td>HDL cholesterol (mg/dL)</td>
<td>47.5±12.7</td>
<td>43.8±12.1</td>
</tr>
<tr>
<td>HDL triglycerides (mg/dL)</td>
<td>33.3±41.9</td>
<td>46.7±61.3</td>
</tr>
</tbody>
</table>

1, 2 p<0.05; after adjustment for age; ** The LDL cholesterol was calculated from the Friedewald equation. * The HDL cholesterol was measured by the alternative method of precipitation with phosphotungstic acid.
Table 4

Differences in the genotype distribution (%) of the polymorphisms of the cluster classified as the presence or absence of some mutation in the two polymorphisms of the apolipoprotein AI studied by χ² square test in controls and patients with gout

<table>
<thead>
<tr>
<th></th>
<th>No mutation</th>
<th>At least one mutation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Controls (n=139)</td>
<td>58.3</td>
<td>41.7</td>
</tr>
<tr>
<td>Patients (n=52)</td>
<td>36.5</td>
<td>63.5</td>
</tr>
</tbody>
</table>

p=0.007
Tabla 5

Means of the biological variables in patients with gout according to the presence or absence of some mutation in the apolipoprotein AI-CIII-AIV cluster

<table>
<thead>
<tr>
<th></th>
<th>No mutation</th>
<th>At least one mutation</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>19</td>
<td>33</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>29.9±8.0</td>
<td>27.5±9.0</td>
</tr>
<tr>
<td>Uric acid (mg/dL)</td>
<td>8.1±2.1</td>
<td>7.8±1.5</td>
</tr>
<tr>
<td>Cholesterol (mg/dL)</td>
<td>205.9±31.0</td>
<td>218.0±39.9</td>
</tr>
<tr>
<td>Triglycerides (mg/dL)</td>
<td>248.1±221.0</td>
<td>261.0±260.0</td>
</tr>
<tr>
<td>Glycemia (mg/dL)</td>
<td>112.0±27.5</td>
<td>107.0±14.0</td>
</tr>
<tr>
<td>Uric acid clearance (ml/min)</td>
<td>5.0±2.9</td>
<td>4.9±2.7</td>
</tr>
<tr>
<td>Excretory fraction</td>
<td>5.5±1.7</td>
<td>6.1±1.9</td>
</tr>
<tr>
<td>VLDL cholesterol (mg/dL)</td>
<td>9.4±7.7</td>
<td>18.5±14.0ᵃ</td>
</tr>
<tr>
<td>VLDL triglycerides (mg/dL)</td>
<td>24.7±14.7</td>
<td>39.6±25.0ᵇ</td>
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<tr>
<td>LDL cholesterol (mg/dL)</td>
<td>89.5±26.5</td>
<td>88.8±32.9</td>
</tr>
<tr>
<td>LDL triglycerides (mg/dL)</td>
<td>18.0±6.0</td>
<td>18.4±7.7</td>
</tr>
<tr>
<td>IDL cholesterol (mg/dL)</td>
<td>6.8±3.1</td>
<td>11.7±9.8ᶜ</td>
</tr>
<tr>
<td>IDL triglycerides (mg/dL)</td>
<td>6.4±2.1</td>
<td>8.3±5.7</td>
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<tr>
<td>HDL cholesterol (mg/dL)</td>
<td>32.3±5.7</td>
<td>36.9±9.3</td>
</tr>
<tr>
<td>HDL triglycerides (mg/dL)</td>
<td>11.2±5.1</td>
<td>10.4±4.8</td>
</tr>
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</table>

ᵃp=0.044;ᵇp=0.014;ᶜp=0.021
Contribution of polymorphisms in the apolipoprotein AI- CIII-AIV cluster to hyperlipidaemia in patients with gout

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