ACE insertion deletion polymorphisms and effectiveness of statin therapy

We read with great interest the data reported by Kastelein et al. concerning the effect of the ACE deletion/insertion (D/I) genotypes on the effectiveness of HMG-CoA reductase inhibitors in primary and secondary prevention in patients with hypercholesterolaemia [1]. In details, the above authors suggested that in subjects with two I alleles, the effectiveness of statins on primary and secondary prevention was highest, while in subjects with two D alleles no effectiveness was demonstrated. On the contrary, Marian et al. reported higher lipid lowering effect of statin therapy in patients with the D allele compared to those with the I allele [2]. We have studied the effect of the ACE D/I genotypes on the lipid lowering effect of statin therapy in patients with molecularly defined heterozygous familial hypercholesterolaemia (FH). In details, atorvastatin 20 mg/day was prescribed in 49 patients with heterozygous FH. In all cases blood samples were obtained after a 14-h overnight fast for the determination of lipid parameters before and after 12 weeks of drug administration. ACE genotyping was done using a previously described protocol [3]. The results of our study showed no interaction between the ACE genotypes and the LDL-cholesterol lowering effect of statin therapy in patients with FH. In details, the percent decrements in LDL-cholesterol were 37 ± 10 in patients with the DD genotype, 40 ± 10 in patients with the DI genotype and 38 ± 8 in patients with the II genotype [p = 0.44, by analysis of covariance taking into account the baseline LDL-cholesterol levels as covariate (ANCOVA)] (Table 1). Interestingly, the ACE genotypes did not affect the lipid lowering response of atorvastatin after adjustment for the type of the LDL receptor gene mutation [receptor negative (n = 28) versus receptor defective (n = 21) mutations] as well as for the apolipoprotein (apo) E gene polymorphisms (ε2, ε3 and ε4 alleles) (data not shown). In conclusion, the data concerning the effect of ACE D/I polymorphism on the lipid lowering effect of statin therapy are diverse. Other genetic markers or environmental factors may influence the interaction of the ACE D/I polymorphism and the lipid lowering effect of statins in patients with hypercholesterolaemia.

Table 1

<table>
<thead>
<tr>
<th>ACE genotypes</th>
<th>Number of patients (n)</th>
<th>Decrease in LDL-C (%) (mean ± S.D.)</th>
<th>p-Valuea</th>
</tr>
</thead>
<tbody>
<tr>
<td>DD</td>
<td>17</td>
<td>37 ± 10</td>
<td>0.44</td>
</tr>
<tr>
<td>DI</td>
<td>25</td>
<td>40 ± 10</td>
<td>0.28</td>
</tr>
<tr>
<td>II</td>
<td>7</td>
<td>38 ± 8</td>
<td>0.31</td>
</tr>
</tbody>
</table>

a By ANCOVA.

References


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1 September 2004
Available online 8 December 2004

doi:10.1016/j.atherosclerosis.2004.10.003