Macrolide Treatment Does Not Influence Serum Homocysteine in Chlamydia pneumoniae-seropositive Patients Suffering from Atherosclerosis

To the Editor:

Both chronic infection with Chlamydia pneumoniae and hyperhomocysteinemia are assumed to increase the atherosclerotic risk (1, 2). Recently, we reported that C. pneumoniae seropositivity is linked with hyperhomocysteinemia in male patients suffering from established atherosclerosis (3). However, the nature of the relationship between the two risk factors is still elusive.

To further investigate the relationship between C. pneumoniae seropositivity and hyperhomocysteinemia, we randomly assigned 40 C. pneumoniae-seropositive men suffering from peripheral arterial occlusive disease to receive either roxithromycin (300 mg daily) or placebo for 1 month. We selected elderly men (71.3 ± 8.4 years) with a high prevalence of smoking (>80%) and at high risk of undergoing progression of atherosclerotic disease as the study population. Exclusion criteria were diabetes mellitus, malignant neoplasia, chronic inflammatory disorders, and renal insufficiency. Testing for antibodies against C. pneumoniae was performed by a microimmunofluorescence assay (MRL). C. pneumoniae seropositivity was defined as an IgG titer ≥1:128. Fasting serum homocysteine was determined by HPLC (Bio-Rad) at baseline, at the end of the treatment period, and 6 months after the study medication was ended. As shown in Table 1, homocysteine concentrations, which were moderately increased in both study groups, were not influenced by antibiotic treatment. However, roxithromycin treatment had a substantial (beneficial) effect on the clinical course of peripheral arterial occlusive disease and on carotid plaque size in these patients (4).

Macrolide treatment, although preventing progression of the atherosclerotic disease, had no influence on homocysteine concentrations. This finding makes it improbable that C. pneumoniae infection directly causes hyperhomocysteinemia. The following two hypotheses provide more probable explanations for the association between C. pneumoniae seropositivity and hyperhomocysteinemia: either (a) chronic endovascular infection with C. pneumoniae causes, at least in advanced atherosclerosis, irreversible cell injury that is responsible for persistent hyperhomocysteinemia by an as yet unknown mechanism; or (b) preexisting hyperhomocysteinemia, possibly accompanied by decreased methionine concentrations, represents a metabolic niche favoring chronic infection with C. pneumoniae. In vitro, the growth of C. pneumoniae is known to be enhanced in media depleted of lysine and methionine (5).

Table 1. Influence of roxithromycin treatment on serum homocysteine. a

<table>
<thead>
<tr>
<th>Homocysteine, μmol/L</th>
<th>Roxithromycin (n = 20)</th>
<th>Placebo (n = 20)</th>
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<tbody>
<tr>
<td>At baseline</td>
<td>23.8 ± 15.2</td>
<td>22.6 ± 8.2</td>
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<tr>
<td>After 1 month of treatment</td>
<td>25.2 ± 15.5</td>
<td>21.9 ± 9.7</td>
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<tr>
<td>After 6 months</td>
<td>24.8 ± 16.1</td>
<td>21.5 ± 7.0</td>
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a Values are the mean ± SD.

References


Georg Schulthess1 a
Friedrich E. Maly2

1 Department of Internal Medicine Medical Policlinic
2 Institute of Clinical Chemistry University Hospital CH-8091 Zurich, Switzerland

a Author for correspondence. Fax 41-1-255-4567; e-mail georg.schulthess@dim.usz.ch.