The 20210 G to A Prothrombin Polymorphism and Late Complications in Type 1 Diabetes Mellitus

Dear Sir,

The hypercoaguable state in diabetes mellitus and its association with late complications is discussed widely. Fibrinogen, Factor VII, Protein C and vWF showed significant positive correlation with the urinary albumin excretion rate (1). Intravascular thrombin generation, hyperreactive platelets and reduced fibrinolytic capacity are also reflecting a prethrombotic situation in diabetes (2). This may relate to changes in the microcirculation resulting in diabetic nephropathy or retinopathy. The clinical appearance and progression of late complications of diabetes can only in part be explained by the quality of metabolic control. Ruiz reviewed the influence of the genetic factors on late complications in diabetes mellitus (3). He suggests that candidate genes affecting lipid metabolism, haemodynamics as well as the coagulation system might explain the excess risk for development of late diabetic complications not explained on the basis of hyperglycemia alone. The heterozygous 20210 G to A prothrombin polymorphism has been described as a risk factor for deep venous thrombosis, arterial disease and myocardial infarction in non-diabetic patients. This genetic variant is associated with elevated levels of prothrombin in plasma (4, 5). Apart from the known effect on macrovascular disease, elevated prothrombin concentrations might have an influence on the appearance or progression of microangiopathy in diabetes mellitus.

We screened 384 type 1 diabetic patients for the 20210 G to A prothrombin polymorphism using PCR amplification with the forward primer 5'-TGGGAAATATGGCTTCTACA-3' and the reverse primer 5'-CACTGGGAGCATTGAA-3' followed by Hind III Restriction Analysis as described by Ferraresi et al. (6). The question was whether there is an association of the genetic prothrombin variant with late complications in type 1 diabetes mellitus. Patient data were available for duration of diabetes, nephropathy (persistent albuminuria > 20 mg/l), retinopathy (diagnosis established by ophthalmologists) and cardiac events (diagnosed by stress ECG, a history of documented myocardial infarction) in the non-diabetic patients. This genetic variant is associated with elevated levels of prothrombin in plasma (4, 5). Apart from the known effect on macrovascular disease, elevated prothrombin concentrations might have an influence on the appearance or progression of microangiopathy in diabetes mellitus.

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Table 1 Late complications in type 1 diabetic patients with and without the 20210 G to A prothrombin polymorphism

<table>
<thead>
<tr>
<th></th>
<th>Nephropathy</th>
<th>Retinopathy</th>
<th>Cardiac Events</th>
<th>No late complications</th>
</tr>
</thead>
<tbody>
<tr>
<td>20210 G -</td>
<td>136</td>
<td>221</td>
<td>35</td>
<td>115</td>
</tr>
<tr>
<td>genotype n = 375</td>
<td>36%</td>
<td>59%</td>
<td>9%</td>
<td>31%</td>
</tr>
<tr>
<td>20210 A -</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>variant n = 9</td>
<td>3</td>
<td>3</td>
<td>1</td>
<td>5</td>
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<tr>
<td></td>
<td>33%</td>
<td>33%</td>
<td>11%</td>
<td>55%</td>
</tr>
</tbody>
</table>

In summary: The 20210 G to A prothrombin variant does not seem to have a major influence on the occurrence of coronary heart disease, nephropathy or retinopathy in type I diabetic patients.

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References