Short report

Proinsulin and insulin responses to a mixed meal in hypertriglyceridaemic men

Abstract

Aim—To investigate the contribution of proinsulin to the “hyperinsulinæmia” of hypertriglyceridaemia.

Methods—Plasma glucose, triglyceride, immunoreactive insulin, and intact proinsulin concentrations were measured before and after a mixed meal in 11 hypertriglyceridaemic men and six healthy normotriglyceridaemic male controls.

Results—Hypertriglyceridaemic subjects had greater fasting (101 vs 50 pmol/l) and integrated (139 vs 81 × 10−3 pmol/l/h) insulin concentrations than controls. Fasting and integrated glucose and proinsulin concentrations were similar in the two groups.

Conclusions—Proinsulin does not contribute to the hyperinsulinæmia observed in hypertriglyceridaemic subjects and is therefore unlikely to contribute to the increased cardiovascular risk associated with hypertriglyceridaemia.

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Keywords: hypertriglyceridaemia; insulin; proinsulin

Hypertriglyceridaemia and postprandial lipaemia are risk factors in the development of coronary artery disease.1 Hypertriglyceridaemia is characterised by hyperinsulinæmia which until recently has been defined by insulin assays using polyclonal antiserum in which lower biological activity proinsulin and partially processed proinsulin cross react.2 It has been shown that apparently hyperinsulinæmic patients with type 2 (non-insulin-dependent) diabetes mellitus are insulin deficient but hyperproinsulinaemic.3 It is therefore possible that proinsulin could contribute to the hyperinsulinæmia of hypertriglyceridaemia. This may be of importance since hyperproinsulinaemia has been associated with increased cardiovascular risk4–6 and may partly explain the increased cardiovascular morbidity reported in hypertriglyceridaemia. There are, however, few data on plasma proinsulin levels in hypertriglyceridaemic subjects with normal glucose tolerance; in particular the contribution of proinsulin to the postprandial hyperinsulinæmia of hypertriglyceridaemia has not been studied before. We therefore measured plasma glucose, triglyceride, insulin, and proinsulin concentrations before and after a mixed meal for four hours in 11 hypertriglyceridaemic men and in six healthy normotriglyceridaemic male controls.
Fasting and integrated triglycerides correlated with fasting insulin \((r = 0.62, p = 0.009)\) and with integrated insulin \((r = 0.54, p = 0.026)\) and fasting triglycerides \((r = 0.57, p = 0.017)\). Integrated triglycerides correlated with age \((r = 0.66, p = 0.004)\), integrated insulin \((r = 0.54, p = 0.026)\), and fasting proinsulin \((r = 0.69, p = 0.002)\), and integrated proinsulin \((r = 0.57, p = 0.017)\). Integrated proinsulin correlated with integrated proinsulin \((r = 0.64, p = 0.006)\). There were no other correlations.

### Table 1
Characteristics of hypertriglyceridaemic men and male controls, and their plasma triglyceride, glucose, insulin, and proinsulin responses during a mixed meal

<table>
<thead>
<tr>
<th>Variable</th>
<th>Controls</th>
<th>Hypertriglyceridaemic men</th>
<th>(p) Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>6</td>
<td>11</td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>36.8 (26.3 to 47.4)</td>
<td>42.0 (35.3 to 48.7)</td>
<td>0.301</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>27.1 (24.7 to 28.8)</td>
<td>27.0 (25.7 to 28.1)</td>
<td>0.858</td>
</tr>
<tr>
<td>Fasting plasma cholesterol (mmol/litre)</td>
<td>6.1 (4.4 to 8.0)</td>
<td>7.0 (5.9 to 7.8)</td>
<td>0.350</td>
</tr>
<tr>
<td>Fasting plasma triglyceride (mmol/litre)</td>
<td>1.3 (0.8 to 1.8)</td>
<td>5.5 (3.9 to 9.3)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Integrated triglycerides (mmol/litre/h)</td>
<td>399 (160 to 709)</td>
<td>1506 (1123 to 2286)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Fasting glucose (mmol/litre)</td>
<td>4.8 (4.0 to 5.4)</td>
<td>5.2 (4.9 to 5.4)</td>
<td>0.078</td>
</tr>
<tr>
<td>Integrated glucose (mmol/litre/h)</td>
<td>1332 (1198 to 1677)</td>
<td>1568 (1472 to 1791)</td>
<td>0.149</td>
</tr>
<tr>
<td>Fasting insulin (pmol/litre)</td>
<td>50 (25 to 73)</td>
<td>101 (56 to 235)</td>
<td>0.030</td>
</tr>
<tr>
<td>Integrated insulin (pmol/litre/h)</td>
<td>8 (52 to 102)</td>
<td>139 (100 to 223)</td>
<td>0.020</td>
</tr>
<tr>
<td>Fasting proinsulin (pmol/litre)</td>
<td>15 (5 to 27)</td>
<td>14 (10 to 19)</td>
<td>0.961</td>
</tr>
<tr>
<td>Integrated proinsulin (\times 10^{-3}) (pmol/litre/h)</td>
<td>9.9 (2.4 to 19.8)</td>
<td>10.3 (5.7 to 19.7)</td>
<td>0.999</td>
</tr>
</tbody>
</table>

Values are medians (95% confidence intervals).

BMI, body mass index.

Discussion

We have confirmed that hypertriglyceridaemic subjects have fasting and stimulated hyperinsulinemia. The similar proinsulin concentrations in hypertriglyceridaemic subjects and their controls suggest that proinsulin hypersecretion does not contribute to their fasting or postprandial hyperinsulinaemia. It is possible that 31/32 split proinsulin (which does not cross react in this proinsulin assay) could contribute to the hyperinsulinaemia but this is unlikely as raised 31/32 split concentrations are usually associated with hyperproinsulinaemia. Although hyperproinsulinaemia has been reported in hypertriglyceridaemic subjects with type 2 diabetes mellitus, this is probably related to their glucose intolerance rather than their hypertriglyceridaemia. Since hypertriglyceridaemic subjects with normal glucose tolerance have normoproinsulinaemia it is unlikely that proinsulin contributes to the increased cardiovascular morbidity associated with hypertriglyceridaemia.

In summary proinsulin does not contribute to the hyperinsulinaemia observed in hypertriglyceridaemic subjects and therefore the increased cardiovascular morbidity associated with hypertriglyceridaemia is unlikely to be caused by altered proinsulin concentrations.

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R Gama, F Norris, S Hampton, L Morgan, J Wright and V Marks

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