The lipidomic signature of disease progression in nonalcoholic fatty liver disease

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BACKGROUND & AIM

Nonalcoholic fatty liver disease (NAFLD) includes a spectrum of histological phenotypes including isolated steatosis, steatosis with inflammation and full-blown steatohepatitis. Each of these phenotypes has been associated with a risk of progression to cirrhosis and liver failure. While biopsy assessment with a liver biopsy is the gold standard for assessment of disease progression it is fraught with limitations such as sampling variability and its invasive nature. There is therefore a major unmet need to identify a signature of disease progression that does not rely on a liver biopsy.

Metabolomics provides an unbiased approach to obtain an assessment of whole-body metabolic response to disease progression. Previous attempts at describing a lipid signature focused on fatty liver versus nonalcoholic steatohepatitis (NAFLD) versus NAFLD. The lipidomic signature of disease progression over earlier stages thus remains unknown.

The aim of this study is to characterize the changes in the circulating lipid metabolomes with disease progression from non-fatty to advanced fibrosis in subjects with NAFLD.

METHODS

Ninety-six plasma samples collected at the time of liver biopsy were analyzed by ultra-performance liquid chromatography coupled to mass spectrometry (UPLC-MS). Specifically, amino acids, fatty acids, bile acids, glycoprophosphatidylinositol, sphingolipids, glycosphosphatidylinositol, and steroids were analyzed using three different platforms.

RESULTS

Plasma samples were classified according to the disease progression in NAFLD as control, NAFLD with no fibrosis, NAFLD with early stage of fibrosis (stage 1-2) and NAFLD with advanced fibrosis (stage 3-4).

<table>
<thead>
<tr>
<th>Clinical data</th>
<th>Control</th>
<th>NAFLD with no fibrosis</th>
<th>NAFLD F1–2</th>
<th>NAFLD F3–4</th>
</tr>
</thead>
<tbody>
<tr>
<td>N (patients)</td>
<td>11 (7)</td>
<td>29 (15)</td>
<td>43 (22)</td>
<td>22 (17)</td>
</tr>
<tr>
<td>Age</td>
<td>49.6 ± 9.5</td>
<td>48.9 ± 11.9</td>
<td>50.4 ± 10.5</td>
<td>50.5 ± 7.6</td>
</tr>
<tr>
<td>Total cholesterol (mg/dL)</td>
<td>178.0 ± 40.6</td>
<td>192.6 ± 44.6</td>
<td>186.1 ± 49.8</td>
<td>195.5 ± 43.5</td>
</tr>
<tr>
<td>Triglyceride (mg/dL)</td>
<td>140.2 ± 68.2</td>
<td>156.1 ± 70.1</td>
<td>201.8 ± 113.0</td>
<td>165.3 ± 127.1</td>
</tr>
<tr>
<td>Glucose (mg/dL)</td>
<td>93.2 ± 20.1</td>
<td>103.0 ± 24.4</td>
<td>111.1 ± 41.9</td>
<td>125.3 ± 47.7</td>
</tr>
<tr>
<td>AST (aIU/L)</td>
<td>74.2 ± 63.0</td>
<td>45.7 ± 37.3</td>
<td>60.1 ± 39.1</td>
<td>65.5 ± 34.2</td>
</tr>
<tr>
<td>ALT (aIU/L)</td>
<td>101.1 ± 75.6</td>
<td>58.8 ± 57.3</td>
<td>82.6 ± 11.4</td>
<td>84.5 ± 48.5</td>
</tr>
</tbody>
</table>

Mean ± SD

Twenty-two primary metabolites, out of the 502 analyzed, were associated with NAFLD progression.

REFERENCES


DISCLOSURES

Puneet Puri - Advisory Committees or Review Panels: Health Diagnostic Laboratory Inc.; Consulting: NPS Pharmaceuticals Inc., Jose M. Mato - Stock shareholder: OWI

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