Probiotics: a possible role in treatment of adult and pediatric non alcoholic fatty liver disease

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LETTER TO EDITOR

Dear Editor:

Sir, we read with much interest the Concise Review by Doctors Machado and Cortez-Pinto on gut microbiota and nonalcoholic fatty liver disease (NAFLD) appearing in the July-August issue of Annals of Hepatology.1 The Authors correctly pointed out that, based on preliminary experiments on different NAFLD animal models and different bacterial strains of probiotics, it would be expected that interventions which modulate intestinal microbiota may be beneficial also in human obesity related liver dysfunction. In this regard they mentioned the two non-randomized pilot studies2,3 quoted by the Cochrane meta-analysis of Lirussi, et al.4 as the only meager evidence available at present.

We would suggest to consider that results of the first one,2 however, are strongly puzzled by co-treatment with prebiotics and antioxidants, i.e. two other alleged components of NAFLD therapeutic arsenal.5 The second study,3 instead, investigated the outcome of liver dysfunction parameters and oxidative stress markers using probiotics as the single treatment in different categories of adult chronic liver disease including only a subgroup of NAFLD patients for whom liver function tests data were not shown.

Here we recommend, therefore, to contemplate also two other recent pilot, double blind, randomized clinical trials6,7 which appeared subsequent to 2007 meta-analysis by Lirussi. These studies compare in table 1.

The first RCT6 evaluated the effects of a 12 week course treatment with 500 million of Lactobacillus bulgaricus and Streptococcus thermophiles/day in adult patients with biopsy proven NAFLD. Even though anthropometric parameters and cardiovascular risk factors remained unchanged in both treated and control groups, probiotic treatment resulted in a significant improvement of aminotransferases levels.

The second RCT7 was carried out by our group in obese children with NAFLD unable to comply with lifestyle interventions. We showed that a short (8 weeks) course of probiotic treatment with Lactobacillus GG (12 billion CFU/day), irrespective of changes in BMI z score and visceral fat, determined a significant decrease (with normalization in 80% of cases) in alanine aminotransferase values. This was associated also to a significant reduction of anti peptidoglycan-polysaccharide antibodies (i.e. an alleged small intestinal bacterial overgrowth marker), while tumor necrosis factor-α, and ultrasonographic bright liver parameters remained fairly stable.

Although several aspects of probiotics beneficial action in NAFLD (e.g. type of strain and doses) still need further elucidation, altogether, these other data confirm and strengthen Doctors Machado and Cortez-Pinto preliminary conclusions.1 That is, intestinal flora manipulation warrants consideration as a therapeutic tool to treat obesity related liver dysfunction of adult and pediatric individuals who are noncompliant to its difficult mainstay treatment, i.e. weight loss through slimming diets and lifestyle interventions.5,7

As even minimal weight and lifestyle changes may affect the biochemical and imaging parameters of NAFLD,8 we suggest that future probiotics studies –regardless of an existing controlled harm– should still be designed as short-term trials, strictly registering patients’ anthropometric changes. This precaution will help to circumvent the unpredictable effects of lifestyle changes that have hitherto usually confounded the results of a number of long-term studies with this and other treatments in the challenging obese patients population.5
<table>
<thead>
<tr>
<th>Authors (reference)</th>
<th>Year of publication</th>
<th>Type of study</th>
<th>Number patients/disease</th>
<th>Mean age (years)</th>
<th>Primary end-point</th>
<th>Treatment</th>
<th>Length of treatment</th>
<th>Diet regimen</th>
<th>Anthropometric parameters</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Loguercio, et al. 2</td>
<td>2002</td>
<td>Open label</td>
<td>37 (range 29-56)</td>
<td>44.3 ± 15.1</td>
<td>ALT and GGT variation</td>
<td>Different bacteria and antioxidants.</td>
<td>2 months</td>
<td>Not supervised</td>
<td>Δ ALT: 64.5 ± 26.5%; Δ GGT: 55.2 ± 31.3% (p &lt; 0.01 vs. basal values); Significant decrease (p &lt; 0.01) of ALT and GGT variation, liver echogenicity, cytokines (TNFα, IL6), and lipid peroxidation markers. Decreased lipid peroxidation reduction (p &lt; 0.01) of 60.4 ± 30.4 vs. basal values. ALT normalization (significant value, not shown) MDA, 4-HNE, and S-NO. AST 41.3 ± 15.3 to 35.6 ± 10.4 (p &lt; 0.05); vs. 37% in placebo. GGT: 118.2 ± 63.9 to 107.7 ± 60.8 (p&lt;0.05). Unchanged in placebo group. Cytokines unchanged.</td>
<td>Double blind RCT</td>
</tr>
<tr>
<td>Loguercio, et al. 3</td>
<td>2005</td>
<td>Double blind RCT</td>
<td>27/NAFLD</td>
<td>37 (range 29-56)</td>
<td>ALT and GGT variation</td>
<td>Lactobacillus bulgaricus and Lactobacillus GG</td>
<td>3 months</td>
<td>Not supervised</td>
<td>Δ ALT and PG-PS IgA treated group: 60.4 ± 30.4 (p &lt; 0.01); Δ ALT-64.5 ± 26.5%; Δ GGT: 55.2 ± 31.3% (p &lt; 0.01 vs. basal values); Significant decrease (p &lt; 0.01) of ALT and GGT variation, liver echogenicity, cytokines (TNFα, IL6), and lipid peroxidation markers. Decreased lipid peroxidation reduction (p &lt; 0.01) of 60.4 ± 30.4 (p &lt; 0.05); AST 41.3 ± 15.3 to 35.6 ± 10.4 (p &lt; 0.05); vs. 37% in placebo. GGT: 118.2 ± 63.9 to 107.7 ± 60.8 (p&lt;0.05). Unchanged in placebo group. Cytokines unchanged.</td>
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REFERENCES


