

Natural Approach Against Lipotoxic Traffic in Nonalcoholic Fatty Liver Disease

To the Editor:

We read with great interest the editorial by Bass, recently published in *HEPATOLOGY*.¹ The author, based on the results of a recent article in an earlier issue of *HEPATOLOGY*² and another reference of interest in the last 2 years,³ highlights benefits and chances that the analysis of plasma lipid profile could provide. In these two articles, Puri et al. characterized circulating lipidome in normal subjects and extrapolated the significance of the variations observed in patients with nonalcoholic fatty liver disease (NAFLD). The lipidomic profile of patients with simple steatosis was different from that of lean normal controls, and, more interestingly, it also differed from that observed in subjects with nonalcoholic steatohepatitis (NASH).

All these findings suggest the possibility of drawing a lipid profile which typifies the patients suffering from various forms that characterize NAFLD. However, Bass¹ emphasizes the role of a comprehensive picture of the state of lipid metabolism in NAFLD not only as the basis to expand our knowledge about the molecular pathogenesis of the disease, but also to identify novel diagnostic serum biomarkers and efficient therapeutic natural agents. We would like to stress, in particular, the implications that these works have in therapeutic terms.

Current management of NAFLD includes diet regimen, aerobic exercise, and interventions toward the associated metabolic abnormalities.⁴ Certain nutrients may also be of benefit; in fact, encouraging results demonstrate that antioxidant supplementation may be considered as adjunctive therapy.⁵ Furthermore, in light of remarks made by Bass, it also reinforces the idea that the restoration of normal lipid profile could be one of the major targets of an effective and safe natural therapy for patients with NAFLD. In fact, there are promising data from both animal models and human trials on the use of N-3 long-chain fatty acids (long-chain polyunsaturated fatty acids, or LCPUFAs), including eicosapentaenoic acid and docosahexaenoic acid (DHA), as potential natural treatments for NAFLD.⁶ LCPUFAs are found naturally in fish oil, flaxseed, and some nuts. Interestingly, in a recent clinical trial (registered at <http://clinicaltrials.gov/> with the NCT00885313 identifier), we investigated the effect of dietary supplementation with DHA (250 mg/day) on plasma lipid traffic in children affected by NAFLD. Although the study is still ongoing, unpublished data from the first 6 months of follow-up show that DHA supplementation increases insulin sensitivity, which is paralleled by a reduction in insulin resistance, and decreases fat liver content, thus restoring part of the normal lipidomic profile.

In conclusion, we highlight the importance of adopting a safe and nontoxic new therapy that is able to reverse the metabolic disturbances and the intense lipotoxic traffic in the hepatocytes of patients with NAFLD. The choice of a natural agent such as DHA could be a suitable answer to this need, even if, because the natural history of disease as well as pathogenetic mechanisms are only partly known, further studies are needed to evaluate the potential of DHA to prevent the transition from simple steatosis to NASH.

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