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CORRESPONDENCE

Practice Guidelines on NAFLD

To The Editor:

I read with interest the practice guidelines on nonalcoholic fatty liver disease (NAFLD),[1] in which the authors fail to reference the association between high fructose corn syrup (HFCS) and NAFLD. The intake of HFCS, a combination of glucose and fructose, has increased over time and parallels both the obesity and NAFLD epidemics.[2] Numerous studies demonstrate that the mechanism by which HFCS causes NAFLD is due to fructose. In animal models, fructose causes steatosis and fibrosis[3,4] by either increasing hepatic lipogenesis, causing activation of pyruvate dehydrogenase,[5] activating inflammatory pathways,[6] or up-regulating the expression of sterol regulatory element-binding protein (SREBP).[7]

In humans, excessive fructose intake can lead to increased hepatic lipid deposition, greater insulin resistance, and hypertriglyceridemia.[8] NAFLD patients have been found to drink more HFCS soft drinks compared with healthy controls.[9] A retrospective analysis of 341 NAFLD adults found that those consuming high fructose diets had more fibrosis than those consuming low fructose diets.[10] A prospective controlled trial with histologic endpoints is needed to define the amount of HFCS safe for NAFLD patients and to determine the extent to which fructose contributes to the pathogenesis and progression of NAFLD. However, there are currently sufficient data to recommend that NAFLD patients refrain from excessive consumption of HFCS.

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Potential conflict of interest: Nothing to report.

Reply:

On behalf of my coauthors, I thank Dr. Melissa Palmer, a respected hepatologist, for her interest in the multisociety practice guideline on the diagnosis and management of nonalcoholic fatty liver disease (NAFLD) that was published in the June 2012 issue of Hepatology.[1] Dr. Palmer raises an important issue about the role of fructose and high-fructose corn syrup (HFCS) in the pathogenesis of NAFLD. Dr. Palmer cites several publications that have shown an adverse role for fructose in the experimental models of NAFLD. We do not dispute these published data, but we would like to point out a publication in this journal that argues against a singular role for a high fructose diet in the pathogenesis of NAFLD.[2] Lee et al. showed that although Ossabaw swine fed a high-calorie and high-fructose diet for 24 weeks developed obesity, glucose intolerance, and hypertension, there was no evidence of abnormal liver biochemistries or steatohepatitis until high fat and high cholesterol were also added.[2] This experiment suggested that a diet high in fructose was deleterious in this swine model of steatohepatitis only in combination with a high-fat and high-cholesterol diet.

We agree that prospective human studies with histological endpoints are needed to define the role of fructose and HFCS in the pathogenesis of NAFLD. As a matter of fact, there are ongoing clinical studies investigating the role of high fructose intake in the pathogenesis of human NAFLD and nonalcoholic steatohepatitis. However, there is broad acceptance that excess caloric intake, including those from foods and beverages high in fructose and HFCS play a causal role in obesity. Because the majority of patients with NAFLD and nonalcoholic steatohepatitis are overweight or obese, the avoidance of caloric excess, including that from diets high in fructose and HFCS, will be addressed in the recommendations when the guideline is updated in 2013.

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On behalf of the writing group for the American Association for the Study of Liver Diseases, American College of Gastroenterology, and American Gastroenterology Association practice guideline on the Diagnosis and Management of Nonalcoholic Fatty Liver Disease.

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