Fructose Linked to Fatty Liver Disease

By Charles Bankhead, Staff Writer, MedPage Today
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Review

Daily consumption of fructose -- the sugar commonly found in soft drinks -- significantly increased hepatic fibrosis in patients with nonalcoholic fatty liver disease, according to a study of patients enrolled in a clinical research network.

An adjusted analysis showed high fructose consumption was associated with reduced hepatic steatosis but increased fibrosis stage ($P<0.05$). In older patients, daily fructose consumption increased the risk of hepatic inflammation and hepatocyte ballooning.

"These results identify a readily modifiable environmental risk factor that may ameliorate disease progression in patients with nonalcoholic fatty liver disease (NAFLD)," Manal Abdelmalek, MD, of Duke University, and co-authors reported online in Hepatology.

"Well-designed, prospective controlled dietary interventions studies are necessary to evaluate whether a low-fructose diet improves the metabolic disturbances associated with NAFLD and alters the natural history of NAFLD in those at risk of disease progression," they added.

The rising prevalence of obesity in the U.S. has been accompanied by an increased prevalence of NAFLD. The rapid change in epidemiology suggests environmental factors may contribute to the pathogenesis of NAFLD, the authors wrote.

Several studies have linked both obesity and NAFLD to increased consumption of high-fructose corn syrup, particularly soft drinks. In animal models, fructose induces rapid development of fatty liver and associated leptin resistance, microvascular disease, and vascular inflammation, the authors continued.

Excessive dietary consumption of fructose also has been linked to NAFLD in humans.

Whether fructose consumption influences the transition from NAFLD to nonalcoholic steatohepatitis (NASH) had not been examined carefully. To address that and related issues, Abdelmalek and co-authors analyzed data on 427 adults enrolled in the NASH Clinical Research Network.

Food questionnaire data were collected within three months of enrollment for all patients.

The authors estimated fructose consumption on the basis of patients' self-reported consumption of fruit juices, nondietary sodas, and granulated soft drinks (such as Kool-Aid). Patients were categorized according to weekly fructose consumption: none, less than seven servings weekly, and seven or more servings per week.

By univariate analysis, greater fructose consumption was associated with younger age, male sex, hypertriglyceridemia, low HDL cholesterol, decreased serum glucose, increased caloric intake, and hyperuricemia.

In a multivariate analysis controlling for age, sex, body mass index, and total caloric intake, daily fructose consumption had a significant association with lower steatosis grade and higher fibrosis stage ($P<0.05$ for each).

In a subset analysis of patients ages 48 and older, daily fructose consumption significantly increased the risk of hepatic inflammation ($P<0.05$) and hepatocyte ballooning ($P=0.05$).

In a detailed discussion of their findings, Abdelmalek and colleagues described a process by which high-fructose consumption might influence liver disease.

"The lipogenic and and proinflammatory effects of fructose appear to be attributable to its unique metabolism, which involves a period of transient adenosine triphosphate [ATP] depletion because of its rapid phosphorylation within the cell and from its unique ability among sugars to raise intracellular and serum uric acid," the authors wrote.

They reviewed evidence suggesting that NASH inhibits hepatic adenosine monophosphate kinase, increasing hepatocytes' vulnerability to ATP depletion during fructose metabolism.

"Hence, the presence of hyperuricemia may be a surrogate measure of chronic hepatic ATP depletion in habitual fructose consumers," the authors continued. "In addition, hyperuricemia has long been recognized as a marker of advanced liver disease. More recently, multivariate analysis demonstrated that hyperuricemia is also an independent risk factor for NASH."

Co-author Richard J. Johnson has written a book on the relationship between fructose, obesity, and liver disease and has a patent interest related to lowering uric acid as a means of reducing fatty liver disease