Cigarette smoking, fructose consumption exacerbates liver disease

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Recent studies suggest that modifiable risk factors such as cigarette smoking and fructose consumption can worsen nonalcoholic fatty liver disease (NAFLD). With NAFLD, fat accumulates in the liver of overweight individuals despite drinking little alcohol, causing in some cases liver scarring that can lead to liver failure. Identifying modifiable factors that contribute to disease severity and progression is essential in improving patient outcomes. Details of these studies are published in the May issue of *Hepatology*, a journal of the American Association for the Study of Liver Diseases (AASLD).

NAFLD is the most common cause of liver disease worldwide and research suggests the number of cases will climb given an increasing trend toward higher fat diets, obesity, decreased physical activity, and a rise in diabetes. Past studies indicate that more than 30 million Americans have NAFLD and approximately 8 million may have nonalcoholic steatohepatitis (NASH).

In the first study, Ramón Bataller, M.D., and colleagues from the Hospital Clínic in Barcelona, Spain investigated the effects of cigarette smoking (CS) in obese rats. Rats were divided into 4 groups (n=12 per group): obese smokers, obese non-smokers, control smokers and control non-smokers. Smoker rats were exposed to 2 cigarettes/day, 5 days/week for 4 weeks. Researchers found that obese rats exposed to CS showed a significant increase in ALT serum levels (indicating liver disease), while this effect was not observed in control rats.

"Our results show that CS causes oxidative stress and worsens the severity of NAFLD in obese rats," said Dr. Bataller. "Further studies should investigate longer exposures to CS, and assess whether this finding also occurs in patients with obesity and NAFLD."

In her editorial, also published in *Hepatology* this month, Claudia Zein, M.D., from the Cleveland Clinic, noted that "the importance of these results is that taken together with other experimental and clinical data, they support that cigarette smoking appears to aggravate liver injury in patients with liver disease". Dr. Zein added, "Studies characterizing the effects of cigarette smoking in human NAFLD will be crucial because of the vast number of patients that may benefit from modification of this risk factor."

Additionally, prior studies suggest an over consumption of high fructose corn syrup (HFCS), primarily in the form of soft-drinks, have contributed to weight gain and the rise in obesity, particularly in children and adolescents. Table sugar (sucrose) and HFCS are the two major dietary sources of fructose. Over the past 40 years, consumption of dietary fructose has increased 1,000% according to Bray et al, and doctors believe it to be a major cause of NAFLD.

Researchers from Duke University studied 341 adults enrolled in the NASH Clinical Research Network who responded to a Block food questionnaire within 3 months of a liver biopsy. Fructose consumption was estimated conservatively by including that found in beverages, which accounts for 50% of dietary fructose intake. Results showed that 27.9% of participants consumed at least 1 fructose-containing beverage per day, 52.5% had 1 to 6 beverages with fructose per week, and 19.7% drank no beverages with fructose.

"In patients with NAFLD, daily fructose ingestion was associated with reduced fatty liver (steatosis), but we found increased fibrosis," noted

Manal Abdelmalek, M.D., M.P.H, and lead author of the study. "Further dietary intervention studies are needed to evaluate whether a low-fructose diet improves metabolic disturbances associated with NAFLD and improves patient outcomes for those at risk of disease progression," concluded Dr. Abdelmalek.

A second fructose study led by Ling-Dong Kong, M.D., from Nanjing University in China investigated the effects of curcumin on fructose-induced hypertriglyceridemia and fatty liver in rats. Curcumin, a compound derived from turmeric (curcuma root), is sold as an herbal supplement and is believed to have anti-inflammatory, anti-tumor, and anti-viral properties. Researchers observed a hyperactivity of hepatic protein tyrosine phosphatase 1B (PTP1B), which is associated with defective insulin and leptin signaling, in fructose-fed rats.

For the first time this study demonstrated that curcumin inhibited hepatic PTP1B expression and activity in fructose-fed rats. "Our results provide novel insights into the potential therapeutic mechanisms of curcumin on fructose-induced hepatic steatosis associated with insulin and leptin resistance," said Dr. Kong.

These studies indicate modifying risks such as smoking and fructose consumption offer potential benefits for those with liver diseases. Further studies are needed to explore these benefits in preventing the progression of liver disease.

More information:

Article: "Cigarette Smoking Exacerbates Non-Alcoholic Fatty Liver Disease in Obese Rats." Lorenzo Azzalini, Elisabet Ferrer, Leandra N. Ramalho, Montserrat Moreno, Marlene Domínguez, Jordi Colmenero, Víctor I. Peinado, Joan A. Barberà, Vicente Arroyo, Pere Ginčs, Joan Caballería, Ramón Bataller. Hepatology; Published Online: February 22, 2010 (DOI: 10.1002/hep.23516); Print Issue Date: May 2010.

Editorial: "Clearing the Smoke in Chronic Liver Diseases." Claudia Zein. Hepatology; Published Online: March 26, 2010 (DOI: 10.1002/hep.23694); Print Issue Date: May 2010.

Article: "Increased Fructose Consumption is Associated with Fibrosis Severity in Patients with NAFLD." Manal F. Abdelmalek, Ayako Suzuki, Cynthia Guy, Aynur Unalp-Arida, Ryan Colvin, Richard J. Johnson, Anna Mae Diehl. Hepatology; Published Online: March 17, 2010 (DOI: 10.1002/hep.23535); Print Issue Date: May 2010.

Article: "Curcumin inhibits hepatic protein-tyrosine phosphatase 1B and prevents hypertriglyceridemia and hepatic steatosis in fructose-fed rats." Jian-Mei Li, Yu-Cheng Li, Ling-Dong Kong, Qing-Hua Hu. Hepatology; Published Online: March 10, 2010 (DOI: 10.1002/hep.23524); Print Issue Date: May 2010.

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