Low-carb diets alter glucose formation by the liver

October 20 2008

A new study shows that a low-carbohydrate diet changes hepatic energy metabolism. When carbohydrates are restricted, the liver relies more on substances like lactate and amino acids to form glucose, instead of glycerol. These findings are in the November issue of *Hepatology,* a journal published by John Wiley & Sons on behalf of the American Association for the Study of Liver Diseases (AASLD).

Over the past 30 years, the U.S. population has reduced its fat intake, and increased its consumption of carbohydrates. During the same time period, obesity has been rising along with the prevalence of metabolic liver disease in which fatty deposits in the liver can lead to inflammation, fibrosis and cirrhosis. Some evidence has suggested that a high carbohydrate diet leads to fat formation in the liver, although confirming the association has been difficult.

To better understand hepatic energy production and glucose formation among various types of diets, researchers led by Jeffery Browning of the University of Texas Southwestern Medical Center measured the sources of hepatic glucose and TCA cycle flux in weight-stable subjects, and in subjects following carbohydrate- or calorie-restricted diets.

They recruited 14 subjects whose BMI fell between 25 and 35, and divided them into two groups of seven, matching them for age, BMI, gender and ethnicity. They also included seven lean subjects (BMI

The high-BMI groups followed either a low-carbohydrate or a low-

calorie diet for fourteen days, while the weight-stable group continued their regular diet. All subjects then underwent an overnight metabolic study in which the researchers simultaneously assessed the metabolic pathways of hepatic glucose production and the TCA cycle.

In the weight-stable group, who consumed carbohydrates as a significant proportion of their diet, the TCA cycle alone provided sufficient energy to drive glucose formation. "This was not the case in individuals undergoing carbohydrate restriction," the authors report.

Carbohydrate restriction increased the rate of glucose formed using lactate or amino acids (GNGpep). "This suggests that in fasted human subjects undergoing weight loss, the elevated gluconeogenesis associated with carbohydrate restriction is driven by substrates such as lactate or amino acids," the authors report. In spite of this, TCA cycle flux in the low-carbohydrate group was similar to the low-calorie group, indicating similar rates of energy generation.

In contrast to previous reports, the present study showed similar hepatic glucose production among the dietary groups. The low-carbohydrate group was able to maintain hepatic glucose production at the levels observed for the weight-stable and low-calorie groups by increasing glucose formation using lactate or amino acids to match the reduction in glucose formation from glycerol.

"This observation is reminiscent of 'hepatic autoregulation' by which endogenous glucose production remains unchanged in the setting of altered gluconeogenesis or glycogenolysis because the two pathways tend to compensate for each other," the authors report.

They noted it was interesting that the increased glucose formation using lactate or amino acids in the low-carbohydrate group was not associated with increased TCA cycle flux (i.e. energy production.) However, they

did not measure absolute rates of fatty acid delivery to the liver or ketone body production, limiting their ability to further interpret that finding.

"We have shown that the sources from which endogenous glucose is produced are dependent upon dietary macronutrient composition," the authors write. They suggest that the shift in glucose metabolism associated with a low carbohydrate diet could be beneficial in individuals with non-alcoholic fatty liver disease (NAFLD) due to improved disposal of hepatic fat.

In conclusion, these findings may partly explain the correlation between carbohydrate intake and severity of liver disease in individuals with NAFLD.

Source: Wiley