

Fatty Liver Is Independent Marker of Heart Risk

BY SARA FREEMAN

FROM THE ANNUAL MEETING OF THE EUROPEAN ASSOCIATION FOR THE STUDY OF DIABETES

LISBON – Increasing accumulation of fat, inflammation, and fibrosis of the liver appears tied to corresponding increases in the risk of cardiovascular disease, especially in patients with diabetes, according to the findings of a small retrospective study presented at the meeting.

“What we are realizing is that [nonalcoholic fatty liver disease] is adding extra cardiovascular risk to people with diabetes, and to those without, on top of that which is already existing,” Dr. Christopher Byrne, one of the lead study investigators, said in an interview.

Dr. Byrne, professor of endocrinology and metabolism at the University of Southampton (England), said that patients with documented liver disease may require more aggressive therapies to address the added risk. Such therapies need to target the liver as much as the heart.

In the study of 112 patients with biopsy-proven nonalcoholic fatty liver disease (NAFLD), Kleiner scores – a histologic measure of NAFLD severity – were



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DR. BYRNE

highly correlated with both Framingham Risk Score (FRS) and QRISK2, two cardiovascular risk calculators.

“Nonalcoholic fatty liver disease represents a spectrum of fat-mediated liver conditions causing progressive hepatocellular damage,” said Sarah Hudson, a 5th-year medical student at the University of Southampton.

“There is increasing evidence of an increased cardiovascular risk associated with progression of nonalcoholic fatty liver disease,” Ms. Hudson explained, noting that the preferred method of determining NAFLD severity was via histopathologic assessment.

The aim of the study was to see if a histopathologic marker – Kleiner score – correlated with cardiovascular risk, and if scores were higher in people already known to have a high cardiovascular risk, namely those with diabetes.

Kleiner scores assess the degree of steatosis, lobular inflammation, hepatocyte “ballooning,” and fibrosis, with higher scores indicating more severe liver disease (Hepatology 2005;41:1313-21).

The mean age of the study cohort was 48 years and the mean Kleiner score was 5.3. The median FRS was 13 and the median QRISK2 score was 8. The mean body mass index of participants was approximately 34 kg/m².

Kleiner scores were not only found to be highly correlated with both cardiovas-

cular risk models used, but they were also higher in a subgroup of 32 patients with diabetes when compared with those without diabetes (6.4 vs. 4.7, *P* less than .001).

The increased risk of cardiovascular disease in correlation with increasing NAFLD severity was found to be independent of both hyperglycemia and increasing body weight.

“We need more prospective studies to see what markers may be used to help

stratify who requires biopsy and how best to manage people who have got NAFLD.” Nonalcoholic steatohepatitis was associated with the highest cardiovascular risk estimates in the study.

“Up until now we’ve been very poor in providing cardiovascular risk reduction treatments for patients with NAFLD,” Dr. Byrne said. Currently the only treatment strategy proven to work for NAFLD is lifestyle changes.

“We know that losing weight and increasing activity levels are very effective at decreasing liver fat,” Dr. Byrne explained. “But what we don’t know is whether those lifestyle changes are good at decreasing liver inflammation, or decreasing liver fibrosis.”

Treatment to decrease liver fat and prevent progression to fibrosis is thus urgently needed, and Dr. Byrne is part of a team now looking at the use of a high

For adult patients with type 2 diabetes in addition to diet and exercise

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Important Safety Information for ONGLYZA

Warnings and Precautions

- **Use with Medications Known to Cause Hypoglycemia:** Insulin secretagogues, such as sulfonylureas, cause hypoglycemia. Therefore, a lower dose of the insulin secretagogue may be required to reduce the risk of hypoglycemia when used in combination with ONGLYZA
- **Macrovascular Outcomes:** There have been no clinical studies establishing conclusive evidence of macrovascular risk reduction with ONGLYZA or any other antidiabetic drug

Most Common Adverse Reactions

- Most common adverse reactions (regardless of investigator assessment of causality) reported in ≥5% of patients treated with ONGLYZA and more commonly than in patients treated with control were upper respiratory tract infection (7.7%, 7.6%), headache (7.5%, 5.2%), nasopharyngitis (6.9%, 4.0%) and urinary tract infection (6.8%, 6.1%).
- When used as add-on combination therapy with a thiazolidinedione, the incidence of peripheral edema for ONGLYZA 2.5 mg, 5 mg, and placebo was 3.1%, 8.1% and 4.3%, respectively.

Laboratory Tests

There was a dose-related mean decrease in absolute lymphocyte count observed with ONGLYZA.

Drug Interactions

Because ketoconazole, a strong CYP3A4/5 inhibitor, increased saxagliptin exposure, the dose of ONGLYZA should be limited to 2.5 mg when coadministered with a strong CYP3A4/5 inhibitor (e.g., atazanavir, clarithromycin, indinavir, itraconazole, ketoconazole, nefazodone, nelfinavir, ritonavir, saquinavir, and telithromycin).

VITALS

Major Finding: Mean Kleiner scores were higher in patients with diabetes than in those who did not have diabetes (6.4 vs. 4.7; *P* less than .001).

Data Source: Retrospective study of 112 patients with biopsy-proven NAFLD linking severity of disease with the Framingham Risk Score and QRISK2; 32 had diabetes mellitus.

Disclosures: The study was funded by the National Institute for Health Research and Diabetes UK. Dr. Byrne and Ms. Hudson said they had no relevant financial disclosures. Dr. Byrne has given lectures on behalf of pharmaceutical companies in the past, including Pfizer.

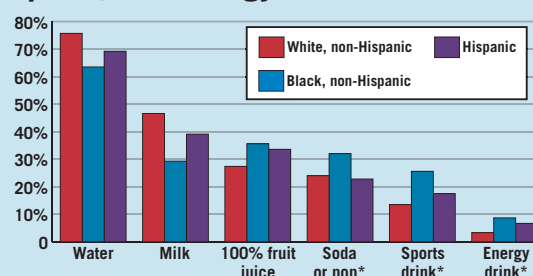
concentration of highly purified omega-3 fatty acid ethyl esters to treat NAFLD.

The highly purified fish oil being used in the trial has been available commer-

cially in Europe for at least a decade (Omacor) and in the United States since 2004 (Lovaza), and is currently licensed to treat hypertriglyceridemia. ■

DATA WATCH

Black High School Students Consume More Soda, Sports, and Energy Drinks Than Do Whites, Hispanics



Source: MMWR 2011;60:778-80

*Not including diet forms.

Note: Based on interviews with 11,429 students for the 2010 National Youth Physical Activity and Nutrition Study.

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Use in Specific Populations

- **Patients with Renal Impairment:** The dose of ONGLYZA is 2.5 mg once daily for patients with moderate or severe renal impairment, or with end-stage renal disease requiring hemodialysis (creatinine clearance [CrCl] \leq 50 mL/min). ONGLYZA should be administered following hemodialysis. ONGLYZA has not been studied in patients undergoing peritoneal dialysis. Assessment of renal function is recommended prior to initiation of ONGLYZA and periodically thereafter.
- **Pregnant and Nursing Women:** There are no adequate and well-controlled studies in pregnant women. ONGLYZA, like other antidiabetic medications, should be used during pregnancy only if clearly needed. It is not known whether saxagliptin is secreted in human milk. Because many drugs are secreted in human milk, caution should be exercised when ONGLYZA is administered to a nursing woman.
- **Pediatric Patients:** Safety and effectiveness of ONGLYZA in pediatric patients have not been established.

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Please read the adjacent Brief Summary of the Product Information.

*Pioglitazone or rosiglitazone

†Based on Tier 2 coverage and the Onglyza Value Card Program.

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Reference: 1. Fingertip Formulary® data as of March 18, 2011. Data on File, March 2011.



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