Diabetes May Raise Risk Of Hepatocellular Cancer

BY BRUCE JANCIN

DENVER — Diabetes appears to be an independent risk factor for hepatocellular carcinoma, with the risk rising as duration of the endocrine disease increases, according to an ongoing, prospective case-control study.

Also, the magnitude of risk for hepatocellular carcinoma (HCC) seems to vary substantially with the type of diabetes treatment used. The risk is greatest in patients on sulfonylureas, lowest in those on thiazolidinediones, and intermediate in insulin-treated patients, Dr. Manal M. Hassan reported at the annual meeting of the American Association for Cancer Research.

Dr. Hassan, of the department of gastrointestinal medical oncology at M.D. Anderson Cancer Center, Houston, presented results from a prospective study involving 420 patients with HCC and 1,109 controls who did not have cancer. The prevalence of diabetes was 23.3% among the cancer patients and 10.4% among controls.

In a multivariate logistic regression analysis adjusted for established HCC risk factors such as heavy alcohol consumption, smoking, and hepatitis C infection, as well as for demographic variables, the odds of developing HCC were increased threefold in patients with a 2- to 5-year history of diagnosed diabetes, 4.8-fold for those with a 6- to 10-year diabetes duration, and 6.6-fold for those with more than a 10-year disease duration, compared with nondiabetic individuals.

Subjects on oral hypoglycemic agents had an adjusted 3.6-fold greater risk of HCC than did nondiabetics. The risk of HCC was increased 6.2-fold in insulin-treated patients, 8.7-fold in those on insulin and oral agents, and 28-fold in those managed by diet only.

Among diabetic patients on oral agents, the HCC risk was 20.5-fold greater in those on sulfonylurea drugs than in nondiabetics. In contrast, biguanide therapy was associated with a much lower 2.5-fold increased risk, and thiazolidinediones had a modest 1.3-fold risk, according to Dr. Hassan. ■

FDA Warns About Liver Risks Of Recalled Dietary Supplement

BY ELIZABETH MECHCATIE

Reports of severe liver injuries—including one fatality—associated with Hydroxycut brand dietary supplements have prompted a nationwide product recall, the Food and Drug Administration announced last month. The products are marketed as weight-loss aids, energy-enhancers, low-carbohydrate diet aids, and diuretics.

The 23 reports of hepatic injuries have been in people aged 21-51 years, with no other identifiable cause for liver diseases and who have not appeared to be related to duration of use or dose. Included are cases of asymptomatic hyperbilirubinemia, jaundice, liver damage, liver transplant, and one death—a 19-year-old previously healthy male in 2007 in the U.S. Southwest. The outcome of another patient with liver failure who was on a transplant list is not known, the FDA said in a press briefing to announce the recall. In some cases, stoppage of Hydroxycut consumption resulted in recovery of liver function.

"We urge you to review your cases of hepatitis in order to determine if any may be related to the use of dietary supplements in these patients," the FDA advised in a letter to health care professionals. In most cases, people had no identifiable preexisting medical condition that would predispose them to liver injury. There also have been reports of people with nonhepatic serious side effects associated with use of the products, including seizures, cardiovascular disorders ranging from palpitations to a heart attack, and rhabdomyolysis.

The recall covers 14 different products with the Hydroxycut name, including Hydroxycut Regular Rapid-Release Capsules, Hydroxycut Hardcore Liquid Caplets, Hydroxycut Caffeine-Free Drink Packets, and Hydroxycut Carb Control. Two Hydroxycut products—Hydroxycut Cleanse and Hoodia—which have completely different ingredients, are not affected by the recall, the FDA said.

Although liver damage associated with use of these supplements "appears to be relatively rare," the FDA is warning consumers to immediately stop using these products, which are sold widely in supermarkets, health food stores, online, and on television. Ontario-based manufacturer Iovate Health Sciences Inc. has told the FDA that 2008 sales totaled more than 9 million units of Hydroxycut products, the agency said.

The precise cause of liver damage has not been identified, because the products contain herbs, herbal extracts, chemicals and metals, and other "overlapping" ingredients, making it difficult to pinpoint the specific ingredient or combination of ingredients that cause liver damage, Dr. Linda Katz, interim chief medical officer at the FDA's Center for Food Safety and Applied Nutrition (CFSAN), said during the briefing.

While most of the other 23 reports of Hydroxycut-related liver injury were made known to the FDA before the passage of the legislation, the agency said the rule allowing the agency to inspect the company's adverse event reports directly has been helpful in its investigation. Such inspection is "something we could not do before," said Vasilios Frankos, Ph.D., director of CSFAN's Division of Dietary Supplement Programs. For information, go to the FDA's Med Watch Web site at www.fda.gov/medwatch/safety/2009/safety09.htm#Hydroxycut. ■

Clinical Tool Helps Triage Patients With Pancreatitis

BY DOUG BRUNK

A simple scoring system for identifying patients with acute pancreatitis who do not require intensive care was 98% accurate and took about 30 minutes to complete, according to Dr. Paul Georg Lankisch and his colleagues.

The tool, known as the harmless acute pancreatitis score (HAPS), combines parameters that suggest a patient has a mild form of the disease: absence of rebound tenderness/guarding, normal levels of serum creatinine, and normal hematocrit.

"A physical examination of a patient with acute pancreatitis takes only minutes to find out whether he or she has rebound tenderness and/or guarding," wrote Dr. Lankisch of the University of Göttingen (Germany) and his colleagues (Clin. Gastroenterol. Hepatol. 2009 [doi:10.1016/j.cgh.2009.02.020]). Hematocrit and serum creatinine are laboratory investigations available in every hospital at all times, and the findings are reported in about 30 minutes. Therefore, the HAPS yields a result in about a half-hour.

The authors pointed out that current tests used to determine the severity of pancreatitis "are insufficiently sensitive, too complicated, too expensive, and not available soon enough or not available at all outside specialized centers."

Dr. Lankisch and his colleagues reported on findings from two prospective studies. In an effort to develop an easier way to identify patients with a first attack of acute pancreatitis who do not require intensive care, the researchers studied 394 patients with the condition who were admitted to the department of internal medicine at the Municipal Clinic in Luneburg, Germany, between 1987 and 2003.

A severe disease course was defined as presence of necrosis by contrast-enhanced CT (a Balthazar score of 5 or more points), while a nonsevere, "harmless" course was defined as having no necrosis (a Balthazar score of 0-4), no need for artificial ventilation or dialysis at any time during the hospital stay, and no fatal outcome.

Of the 394 patients, 143 had rebound tenderness and/or guarding and 251 did not. Baseline characteristics of all patients revealed that absence of rebound tenderness/guarding and normal serum creatinine levels were two strong predictors of a mild disease course. However, 23 of the 251 patients (9%) with no rebound tenderness/guarding and a normal serum creatinine level had a severe course.

The researchers observed that among these 251 patients, hematocrit levels exceeding 43% for men and 39.6% for women were strongly associated with having a severe course of the disease, so they added normal hematocrit levels as a third predictor to form the HAPS.

When applied to the 394 patients, the specificity of the HAPS was 97%, the sensitivity was 29%, the positive predictive value was 98%, and the negative predictive value was 22%.

Dr. Lankisch and his associates then sought to validate the HAPS in a multicenter study of 452 patients with a first attack of pancreatitis seen at one of three clinics between January 2004 and December 2006. These patients were similar to the initial set of patients in terms of pancreatic necrosis, and need for dialysis.

When applied to these patients, the specificity of the HAPS was 97%, the sensitivity was 28%, the positive predictive value was 98%, and the negative predictive value was 18%.

Current tests are insufficiently sensitive, too complicated, too expensive, and not available soon enough or not available at all outside specialized centers.

Combining results from the initial and validation sets of patients revealed that a severe course of disease was seen in only 4 of 204 patients (2%) whose pancreatitis was classified as harmless. "In two patients from the initial set and one from the validation set, the clinical condition deteriorated and for a short time, contrast-enhanced CT demonstrated small but definite areas of necrosis (Balthazar score 6 points)," the researchers reported.

"In the fourth patient, from the validation set, the acute pancreatitis healed without complications, but the patient died of methicillin-resistant *Staphylococcus aureus* pneumonia contracted during his hospital stay. Although the cause of death was unconnected with the pancreatitis, he was assigned to the 'not harmless' group because the fatal infection was acquired during his hospital stay for pancreatitis treatment."

HAPS decides with great accuracy which patients' acute pancreatitis will run a mild course or who will have only interstitial pancreatitis, they concluded.

"Moreover, the score helps to decide which patients do not require intensive management and therapy and expensive imaging procedures, such as contrast-enhanced CT." ■