Novel Weight-Loss Combo May Lower BP

BY DAN HURLEY

FROM THE ANNUAL MEETING OF THE AMERICAN SOCIETY OF HYPERTENSION

NEW YORK — An investigational weight-loss agent that combines two drugs slightly reduced blood pressure in an analysis of three large placebo-controlled clinical trials in a total of 3,985 patients.

The once-daily drug combines a low dose of the generic stimulant phentermine with a low-dose, controlled-release version of the antiepileptic topiramate. The two drugs have been shown previously to cause weight loss by different mechanisms, Dr. Suzanne Oparil said at the meeting.

Higher doses of phentermine are occasionally associated with increased BP, but the combined product appeared to produce enough weight loss—more than 10% of body weight after 56 weeks in two of the studies—to result in modestly lower BP, reported Dr. Oparil, professor of medicine, physiology, and biophysics and director of the vascular biology and hypertension program at the University of Alabama at Birmingham.

"We need a well-tolerated, safe, and effective weight-loss treatment," said Dr. Oparil, who conducted the analysis as a consultant to Vivus, which is developing the combined agent under the brand name Qnexa.

But some physicians at the ASH meeting said they were not entirely convinced of the agent's safety. At the highest dose, a heart rate increase of about 1.5 beats per minute was observed.

The 56-week EQUIP trial enrolled 1,267 obese adults and compared the high-dose combination (phentermine 15 mg and topiramate 92 mg) and a low-dose combination (phentermine 3.75 mg and topiramate 23 mg) with placebo. The 28-week EQUATE trial enrolled 756 obese adults and compared the high-dose formulation and a mid-dose formulation (phentermine 7.5 mg and topiramate 46 mg) with placebo and with the respective single agents. The 56-week CONQUER trial enrolled 2,487 overweight and obese adults with two or more weight-related comorbidities and compared the high- and mid-dose combinations with placebo. Of the 4,510 patients who were initially enrolled in the three trials, 3,985 completed the studies.

In Dr. Oparil's pooled analysis of the three trials, the mean weight loss at week 28 was 1.9% of total body weight for the 1,579 patients on placebo, 5.1% for the 234 patients on the lowest dose of the drug, 8.0% for the 591 patients on the middle dose, and 9.9% for the 1,581 patients on the highest dose. All three active-treatment groups had significantly more weight loss than did the placebo group.

In the two trials that went to 56 weeks, CONQUER and EQUIP, weight loss reached 10.4% of body weight with the highest dose, significantly higher than the 1.5% with placebo.

The reductions in systolic BP in patients on the high-dose combination, compared with placebo, were 3.4 mm Hg after 28 weeks in EQUATE, 3.8 mm Hg after 56 weeks in EQUIP, and 3.2 mm Hg after 56 weeks in CONQUER; all three reductions were significant. Significant reductions in systolic BP also were seen with some of the lower doses of the combined product. For diastolic BP, only two of the higher-dose groups had significantly greater reductions than that seen with placebo. ■

VITALS

Major Finding: In patients on the highest dose of phentermine plus controlled-release topiramate, systolic BP reductions were significantly lower than with placebo: 3.4 mm Hg after 28 weeks in EQUATE, 3.8 mm Hg after 56 weeks in EQUIP, and 3.2 mm Hg after 56 weeks in CONQUER.

Data Source: Pooled analysis of data on 3,985 patients in three clinical trials.

Disclosures: Dr. Oparil disclosed relationships with Vivus and numerous other pharmaceutical companies.

Weight Gain After Age 20 May Raise Colon Adenoma Risk

BY MICHELE SULLIVAN

FROM THE ANNUAL DIGESTIVE DISEASE WEEK

NEW ORLEANS — Adults who have been overweight since early adulthood are nearly twice as likely to have colon adenomas as those with a history of normal weight.

The findings, presented at the annual Digestive Disease Week, reinforce the benefit of maintaining a healthy weight throughout life, Dr. Fritz Francois of New York University wrote in a statement.

They "suggest that the chronicity of obesity is a significant risk factor for developing colon cancer. Given the continued rise in early-onset obesity, especially in minority populations, there is a need for interventions and lifestyle modifications earlier in life to help lessen this serious health risk later in life."

Mr. Ian Fagan, a fourth-year medical student and protégé of Dr. Francois, presented the data during the meeting. The colleagues conducted a prospective study of 1,865 patients who were referred for a screening colonoscopy. Their mean age was 57 years. Body mass index was normal in 38%, whereas 39% were overweight and 23% were obese.

The patients provided information allowing the researchers to estimate their body mass index (BMI) and waist circumference at age 10 and age 20. The investigators compared the past weights to the finding of any adenoma, including advanced neoplasia, during the colonoscopy.

The subjects were divided into three groups: those who had normal weights at age 20 and at present; those who had a normal weight at 20 and were now overweight or obese; and those who had been overweight or obese since age 20.

"Race and ethnicity had a significant impact on weight change since early adulthood," Mr. Fagan said. Sixty-one percent of Hispanics fell into the group that changed from normal weight to overweight or obese, as well as 50% of blacks, 46% of whites, and 7% of Asians.

'Race and ethnicity had a significant impact on weight change since early adulthood.'

MR. FAGAN

Adenomas were significantly more common in patients who had been overweight or obese since age 10 (at a rate of 27%) and in those who went from normal weight to overweight (19%), compared with those who had maintained a normal weight (13%).

After controlling for age, gender, current BMI, U.S. birth, and red meat consumption, the investigators found that becoming overweight or obese in early adulthood almost doubled the risk of an adenoma on screening colonoscopy (odds ratio 1.8). ■

Disclosures: *Neither Mr. Fagan nor Dr. Francois had any potential financial conflicts.*

VITALS

Major Finding: Subjects who became overweight or obese after age 20 were 1.8 times more likely to have colon adenomas than were patients who maintained a normal weight.

Data Source: A prospective study of 1,865 people who underwent a screening colonoscopy.

Disclosures: None.

Insulin Resistance Tied to Barrett's Esophagus Risk

BY HEIDI SPLETE

FROM THE ANNUAL DIGESTIVE DISEASE WEEK

NEW ORLEANS — High insulin levels, insulin resistance, and central body fat were each significantly associated with an increased risk of Barrett's esophagus in a case-control study presented at the meeting.

Previous studies have shown that obesity increases the risk of both esophageal adenocarcinoma and its precursor, Barrett's esophagus. In this study, Dr. Katarina Greer and her colleagues investigated whether central adiposity, hyperinsulinemia, and insulin resistance are independent risk factors for Barrett's esophagus.

"The mechanism through which obesity promotes cancer is still largely unknown," said Dr. Greer of University Hospitals Case Medical Center in Cleveland, Ohio.

The researchers identified 135 adults with Barrett's esophagus from consecutive patients seen at a single tertiary care center. These patients were compared with two adult control groups—135 with gastroesophageal reflux disease (GERD) and 932 controls undergoing routine colonoscopies.

Overall, high levels of insulin and insulin resistance were significant independent risk factors for Barrett's esophagus, Dr. Greer noted. Persons in the highest quartile of serum insulin had a 2.8-fold increase in the risk of Barrett's esophagus, compared with those in the lowest quartile, after adjustment for age, sex, and waist-to-hip ratio.

Regarding insulin resistance, persons in the highest quartile of values for the homeostasis model assessment–insulin resistance (HOMA-IR) were about 3 times more likely to develop Barrett's esophagus than were those in the lowest quartile.

The mean fasting insulin levels were significantly higher in Barrett's esophagus patients than in colonoscopy patients. In addition, Barrett's esophagus patients were more insulin resistant than either of the control groups. The mean HOMA-IR in the Barrett's esophagus group was 2.7, compared with 1.8 in the control groups.

The average BMI was 30.8 kg/m^2 for the Barrett's esophagus patients, 29.6 for the GERD patients, and 29.3 for the controls. The mean waist-to-hip ratio was significantly higher in patients with Barrett's esophagus than in colonoscopy controls. But there was no significant difference in mean waist-to-hip ratio between Barrett's esophagus patients and GERD controls. This suggests that central adiposity may play a role in progression to esophageal cancer, she said.

Disclosures: *Dr. Greer had no financial conflicts of interest.*