

# Combined Regimen Matches Meds for Lower BP

BY MITCHEL L. ZOLER

ORLANDO — Weight loss and exercise were effective complements to a low-salt, low-fat diet for driving down blood pressure in patients with mild hypertension in a controlled study of nearly 150 people.

The combined exercise, weight loss, and healthy-diet regimen led to an average systolic blood pressure reduction of 16 mm Hg during

16 weeks of treatment, Dr. Alan L. Hinderliter said at the annual meeting of the American College of Cardiology.

That amount of blood pressure effect is roughly equivalent to what can be achieved by treatment with one or two antihypertensive medications, said Dr. Steven Nissen, chairman of cardiovascular medicine at the Cleveland Clinic, who was not involved in the study. "This is a spectacular study and shows what can be accomplished with this kind of program. We need now to generalize this" to



everyday practice, Dr. Nissen said. He suggested applying the combined lifestyle regimen to patients who need multiple antihypertensive medications to see if it could eliminate the need for one or more drugs.

The combined lifestyle regimen also led to significant improvements in several other health measures, including aerobic capacity, left ventricular mass, vascular

**Blood pressure reduction was most significant in the diet, exercise, and weight-loss group.**

DR. HINDERLITER

stiffness, and glucose tolerance, said Dr. Hinderliter, a cardiologist at the University of North Carolina, Chapel Hill. "The results reinforce the importance of exercise and weight loss as part of a comprehensive lifestyle modification strategy in people with high blood pressure," he said.

The Exercise and Nutritional Interventions for Cardiovascular Health (ENCORE) study enrolled patients with a blood pressure of 130-159/85-99 mm Hg, aged older than 35 years, with a body mass index of 25-40 kg/m<sup>2</sup>, who did not perform any regular exercise.

Participants could not be on any antihypertensive medication, and did not have secondary hypertension, cardiac disease, diabetes, or chronic kidney disease. The enrollees had an average age of 51, about two-thirds were women, 60% were white, and 40% were African American, and their average BMI was 33 kg/m<sup>2</sup>. Their average blood pressure was 138/85 mm Hg. The study was done at the University of North Carolina, and at Duke University, Durham, N.C.

Dr. Hinderliter and his associates randomly assigned the patients to three treatment groups. Forty-six went on a diet modeled on the one in the Dietary Approaches to Stop Hypertension (DASH) study, which included a high intake of fruits, vegetables, and low-fat dairy products, but which was not designed to result in weight loss. Forty-nine patients began the DASH diet with a reduced calorie level designed to produce weight loss, plus a cognitive-behavioral weight-management program, plus an exercise program that included three sessions per week of supervised exercise. Forty-nine control patients continued their usual care. The DASH diet used by both intervention groups led to significantly reduced in-

take of sodium and fat and a significantly increased intake of potassium and magnesium. Patients in both intervention groups had a high level of compliance with their regimens throughout the study.

After 16 weeks of treatment, the average blood pressure reduction, compared with baseline, the study's primary end point, was 16/10 mm Hg in the total lifestyle modification group, 11/8 mm Hg in the DASH diet-only patients, and 3/4 mm Hg in the control group. Blood pressure in the diet-only group was significantly reduced, compared with the controls, but the decline was even better in the diet, exercise, and weight-loss patients, Dr. Hinderliter reported. The average weight loss in the triple-intervention group was 19 pounds. Those in the diet-only group did not have significant weight loss.

By the end of the study, patients in the complete lifestyle modification group had an average resting blood pressure of 123/76 mm Hg.

The study was funded by the National Heart, Lung, and Blood Institute and Duke University. Dr. Hinderliter said he and his associates had no financial relationships to report. ■

## Obesity to Blame for Rising NAFLD Rate

LA JOLLA, CALIF. — The estimated prevalence of nonalcoholic fatty liver disease in the United States is 10%-33%, and is likely to climb even higher unless Americans start to lose weight.

"Our high body mass index is the main driving force of nonalcoholic fatty liver disease [NAFLD]," Dr. Paul J. Pockros said at a meeting on chronic liver disease sponsored by Scripps Clinic. "The reason we're in trouble is that too many people are eating 2,500 calories at each meal and are not exercising."

The presence of metabolic syndrome or its manifestations can be associated with nonalcoholic steatohepatitis (NASH). In a study of 212 morbidly obese patients who underwent bariatric surgery, 93% had NAFLD, 26% had NASH, and 9% had advanced fibrosis at the time of their surgery (*Obes. Surg.* 2005;15:310-5). Independent predictors of NASH were high aspartate aminotransferase (AST) level, diabetes, and male sex. Independent predictors of advanced fibrosis were high AST, central obesity, and hepatocyte necrosis, said Dr. Pockros, head of the division of gastroenterology and hepatology at Scripps Clinic, La Jolla.

Another study found that patients with NAFLD plus diabetes had higher rates of cirrhosis than did patients who had NAFLD alone (25% vs. 10%, respectively). Overall mortality (risk ratio of 3.3) and mortality related to liver disease (risk ratio of 22.83) were greater in diabetic patients with NAFLD (*Clin. Gastroenterol. Hepatol.* 2004;2:262-5).

Dr. Pockros prescribes a low-fat, Mediterranean-type diet and exercise for his obese patients with NAFLD and NASH. "No single intervention has convincingly improved all important outcomes in NAFLD," he said. "Our best approach is with diet and exercise."

Dr. Pockros said he has received research support from, and is an adviser to, Roche, Vertex, and Gilead, and is an adviser to Amgen.

—Doug Brunk

## Benefits of Brown Adipose Tissue Shown

BY MARY ANN MOON

**B**rown adipose tissue is present in adults and appears to play an active role in metabolism, rather than being vestigial and without physiologic purpose, according to three reports.

Both the presence and the activity of reservoirs of brown adipose tissue seem to be inversely associated with overall adiposity and with measures of the metabolic syndrome, the three studies' investigators said.

"These studies ... are a powerful proof of concept that this tissue might be used as a target for interventions, pharmacologic and environmental, aimed at modulating energy expenditure," Dr. Francesco S. Celi of the National Institute of Diabetes and Digestive and Kidney Diseases said in an accompanying editorial (*N. Engl. J. Med.* 2009;360:1553-6).

Brown adipose tissue helps newborns maintain body temperature but has been thought to regress with age until it is all but lost in adulthood. It was thought to have marginal physiological relevance after infancy. But recent studies using combined PET and CT techniques have suggested that pockets of brown adipose tissue are present in some adults and may be metabolically active in response to cold exposure.

In the first report, Dr. Kirsi A. Virtanen of the University of Turku, Finland, and associates scanned and sampled tissue from putative adipose pockets in five healthy volunteers using PET-CT scanning after cold provocation. Previous research had identified the supraclavicular area as the most prominent site for deposits of brown adipose cells.

Glucose uptake in these pockets increased by a factor of 15 upon exposure to cold, compared with glucose uptake in adjacent white adipose tissue. The pockets of fat also expressed several markers of brown, but not white, adipose tissue, and the biopsy samples showed multilocular, intracellular lipid droplets characteristic of brown fat.

"These findings constitute direct identification of functional human brown adipose tissue," the re-

searchers said. "We speculate that in humans, activated brown adipose tissue has the potential to contribute substantially to energy expenditure," they added (*N. Engl. J. Med.* 2009;360:1518-25).

In the second study, Dr. Aaron M. Cypess of the Joslin Diabetes Center, Boston, and associates analyzed PET-CT images from 1,972 patients who had undergone whole-body scanning for a variety of diagnostic reasons in 2003-2006. They focused on the supraclavicular region after finding that brown adipose tissue had been present in samples from 34 previous patients who had undergone neck surgery for different indications.

They found substantial pockets of brown adipose tissue in 7.5% of women and 3.1% of men, but noted that this likely underestimates the actual prevalence in the general population because the tissue was not being stimulated by exposure to cold at the time of scanning in these subjects (*N. Engl. J. Med.* 2009;360:1509-17).

Dr. Cypess and his colleagues found an inverse correlation between the metabolic activity of brown adipose tissue and subject age, body mass index, and fasting plasma glucose level.

In the third report, Wouter D. van Marken Lichtenbelt, Ph.D., and associates at Maastricht (the Netherlands) University Medical Center used PET-CT to assess cold-stimulated activity of brown adipose tissue in relation to metabolic measures in 24 healthy men. Ten of the men were lean and 14 were overweight or obese.

Brown adipose tissue was present in all but the most obese of these men, a 95% rate that is much higher than has previously been reported. The tissue's activity, measured by energy expenditure at rest and core vs. surface body temperatures, correlated inversely with BMI and percentage of body fat.

Dr. Cypess reported receiving grant support from the Eli Lilly Foundation and being the sole inventor on a pending patent application to use infrared thermography to monitor brown adipose tissue. His study was supported in part by Pfizer, Merck, and the Eli Lilly Foundation. No conflicts of interests were reported by the other researchers. ■