Lifestyle Can Curb CVD Risks in HT Discontinuers

BY SHARON WORCESTER
Southeast Bureau

New Orleans — Lifestyle modifications in postmenopausal women attenuate the adverse effects that discontinuing hormone therapy can have on cardiovascular disease risk factors, findings from a subgroup of participants in the Women on the Move Through Activity and Nutrition (WOMAN) study show.

The study is a 5-year randomized clinical trial designed to evaluate the effects of an aggressive nonpharmacologic lifestyle intervention, including weight loss, dietary modification, and increased physical activity, on measures of subclinical cardiovascular disease. In all, 508 women were randomized to the lifestyle intervention group or to a health education control group for the study, and 240 of these women—the subgroup that was studied in the current analysis—represent those who were taking hormone therapy (HT) at baseline.

Of these 240, 130 discontinued HT within 18 months of study entry, and in these 130 discontinuers, total and LDL cholesterol levels had significantly increased at 18-month follow-up, compared with levels in the 110 participants who remained on HT at 18 months. Stratification by randomized group assignment (the lifestyle modification "intervention" group, or the health education "control" group) in these women—which enabled a comparison between HT continuers and discontinuers in each of the two groups—showed that lifestyle modifications successfully counteract these increases, Kelley K. Pettee, Ph.D., reported in a poster at the annual meeting of the American College of Sports Medicine, and subsequently in the American Journal of Preventive Medicine (Am. J. Prev. Med. 2007;32:483-9).

At 18 months, the 70 HT discontinuers in the intervention group had a mean 4-mg/dL increase in total cholesterol and a mean 7-mg/dL increase in LDL cholesterol, which was not statistically different from the mean 5-mg/dL increase in both total and LDL cholesterol in the 64 HT continuers in the intervention group. However, the 60 HT discontinuers in the control group experienced a mean 22-mg/dL increase in both total and LDL cholesterol, compared with a mean 3-mg/dL increase in total cholesterol and a mean 5-mg/dL increase in LDL cholesterol in the 46 HT continuers in the control group, noted Dr. Pettee, who conducted the research while she was a doctoral candidate at the University of Pittsburgh, but who is currently at Arizona State University, Mesa.

Furthermore, when all 134 women in the intervention group were compared with all 106 in the control group, those in the intervention group experienced significantly greater overall decreases in weight, body mass index, and waist circumference, as well as significantly improved fat intake and increased leisure physical activity, providing further evidence of the benefits of the lifestyle modifications, she reported. (See box.)

WOMAN study participants had a waist circumference of at least 80 cm, and a body mass index (kg/m^2) between 25 and 39.9. They were not taking lipid-lowering drugs, they had an LDL cholesterol level between 100 and 160 mg/dL, and they had no major physical limitations, no known diabetes, and no previously diagnosed psychotic disorder or depression. They had a mean age of 58 years at the 18-month follow-up.

The median duration of HT use prior to study entry did not differ between the continuers and discontinuers, but the groups differed in that continuers were slightly younger and had higher total cholesterol and lower insulin levels. The groups did not differ significantly in regard to anthropometric measures, leisure physical activity, fat intake, or cholesterol, triglyceride, and glucose levels, and they were also similar in regard to education, race, and smoking status.

Those randomized to the control group received a core educational series of six health-related lectures offered during the first year and quarterly thereafter, and those in the lifestyle intervention group worked closely with a team of nutritionists, exercise physiologists, and psychologists who developed individualized diet and exercise programs designed to reduce weight and waist circumference. Those in the intervention group participated in at least 150 minutes per week of moderate-intensity physical activity, and had a caloric intake of 1,300-1,500 calories per day of low total fat and low saturated-fat foods.

Previous studies have shown that lifestyle interventions have a beneficial effect on cardiovascular disease risk factors, but did not account for concurrent changes in HT status, which is "an issue that has become relevant in the post-WHI [Women's Health Initiative] era," Dr. Pettee wrote, referring to the fact that many women discontinued HT following publication of WHI findings that linked HT use with an increased risk of cancer and other health problems. ■

CVD Risk Factor Changes at 18-Month Follow-Up

	Intervention Group	Control Group
Weight	–17 lbs	–2 lbs
BMI (kg/m^2)	–3	–1
Waist circumference	–11 cm	–5 cm
Total cholesterol	5 mg/dL	12 mg/dL
LDL cholesterol	6 mg/dL	14 mg/dL
Saturated fat/cholesterol intake index	19	7
Leisure physical activity	5 MET* hr/wk	1 MET hr/wk

*metabolic equivalent

Note: Based on data from a subgroup of 240 subjects in the WOMAN study.

Source: Dr. Pettee

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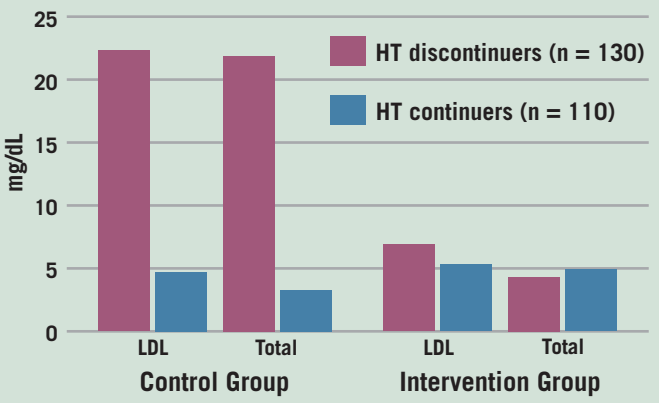
Cholesterol Increases After 18 Months



Note: Based on a subgroup analysis of the WOMAN study.

Source: Dr. Pettee

Elsevier Global Medical News

Some Find Prescribing Chlorthalidone Is Not as Easy as ABC

BY PATRICE WENDLING
Chicago Bureau

Chicago — The diuretic chlorthalidone is being underused in patients with hypertension, despite its superior efficacy—and the reason may be as simple as the lack of a convenient abbreviation for it, according to Dr. William J. Elliot.

Studies support the efficacy of chlorthalidone in reducing hypertension, yet the diuretic hydrochlorothiazide remains favored in clinical practice. One theory is that chlorthalidone is associated with more hypokalemia than hydrochlorothiazide.

But Dr. Elliott, a preventive medicine professor at Chicago's Rush University Medical Center, suggests chlorthalidone has fallen out of favor because, unlike hydrochlorothiazide, which is easily abbreviated as HCTZ, there is no standard abbreviation for chlorthalidone. "It has to be written out, all 14 letters of it," he said at a press briefing at the annual meeting of the America Society of Hypertension.

Dr. Elliott cited several studies favoring chlorthalidone, including a recent blinded randomized head-to-head comparison (Hypertension 2006;47:352-8) that showed a greater reduction in 24-hour mean systolic blood pressure at 8 weeks in patients receiving chlorthalidone 25 mg/day, compared with those receiving HCTZ 50 mg/day (–12.4 mm Hg vs. –7.4 mm Hg, respectively). The greater reduction with chlorthalidone, at half the dose, was thought to be primarily because of its effect on nighttime mean systolic blood pressure, which fell 13.5 mm Hg for chlorthalidone, compared with 6.4 mm Hg for HCTZ.

In the Multiple Risk Factor Intervention Trial (Circulation 1990;82:1616-28), patients who received HCTZ had 44% more coronary heart disease and 16% more deaths after 5 years of follow-up, compared with control patients cared for in the community by primary care physicians. Conversely, there was 58% less coronary heart disease and 41% fewer deaths in patients treated with chlorthalidone, compared with referred-care controls, Dr. Elliott said.

More recently, the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial found fewer cardiovascular events with chlorthalidone than with an angiotensin-converting enzyme inhibitor, and the second Australian National Blood Pressure study found an inhibitor to be superior to HCTZ at reducing combined mortality and morbidity in men, but not women.

"We ought to be putting HCTZ on the list of 'do not use' abbreviations because it is an inferior product and ought to be replaced in general practice by chlorthalidone," he said.

Cost is not a factor in the argument, because both drugs are generically available, said Dr. Elliott, who disclosed possible conflicts of interest with Pfizer Inc., Novartis Pharmaceuticals Corp., AstraZeneca, Kos Pharmaceuticals Co., Abbott Laboratories, and KV Pharmaceutical.

He recommends low-dose chlorthalidone 12.5 mg because of its better efficacy and longer duration of action. He uses diuretics in hypertensive patients with chronic kidney disease, diabetes mellitus, or at high risk of heart failure, but typically switches patients with severe late-stage kidney disease to loop diuretics taken twice daily.

Dr. John Flack, of Wayne State University, in Detroit, told reporters he agreed with Dr. Elliott's recommendation to use chlorthalidone over HCTZ. "It would help if a pharmaceutical company had the courage to break the trend of simply putting HCTZ with everything. They seem reluctant to do it."

HCTZ is part of several fixed-dose combination drugs, but chlorthalidone is available in only three combination products: clonidine (Clorpres), reserpine (Regroton), and atenolol (Tenoretic), Dr. Elliott explained. ■