Metabolic Syndrome and Salt-Sensitive HT Linked

BY ROBERT FINN
San Francisco Bureau

ATLANTA — People with metabolic syndrome have blood pressures that are more sensitive to salt intake than do people without metabolic syndrome, according to a poster presentation by Dr. Luigi X. Cubeddu at a meeting sponsored by the International Society on Hypertension in Blacks.

His study, involving 301 subjects with and without metabolic syndrome, showed that normal dietary salt intake induces large increases in blood pressure in people with metabolic syndrome, rendering them "exquisitely sensitive to dietary salt.

"Salt restriction, in addition to exercise and caloric restriction, must be a fundamental part of the treatment plan for patients with the metabolic syndrome," wrote Dr. Cubeddu of Nova Southeastern University, Fort Lauderdale, Fla. The subjects had a mean age of 42 years, and 109 of them were diagnosed as having metabolic syndrome in accordance with guidelines from the National Cholesterol Education Program. Those with metabolic syndrome had significantly higher baseline blood pressure did than those without: 127/83 mm Hg, compared with 114/75 mm Hg.

The investigators measured blood pressure and several other physiologic signs during a week-long baseline period in which salt intake was normal (8 g/day), and also during a week of high salt intake (about 18 g/day) and a week of low salt intake (2.3 g/day).

The high-salt condition resulted in increases in blood pressure in both groups of subjects, but those with metabolic syndrome had significantly larger increases in both systolic and diastolic pressures. While the patients without metabolic syndrome increased their systolic blood pressure an average of 5.0 mm Hg and their diastolic pressure an average of 3.0 mm Hg, those with metabolic syndrome experienced systolic and diastolic increases of 9.6 and 4.5 mm Hg, respectively.

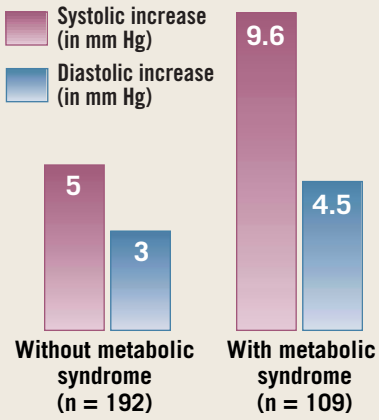
The degree of salt sensitivity was also associated with the severity of metabolic syndrome. The more components of metabolic syndrome a subject had, the larger was his or her decrease in blood pressure associated with salt restriction.

Subjects with four or five components of metabolic syndrome saw decreases of 8.7 mm Hg systolic and 5.0 mm Hg diastolic in response to salt restriction, while those with just two of the traits saw decreases of 3.4 and 2.1, respectively.

The investigators noted that salt sensitivity is a gradual condition that worsens in parallel with metabolic syndrome. Dietary salt is a major determinant of the increased prevalence of prehypertension and hypertension in those with metabolic syndrome.

The meeting was cosponsored by the American Society of Hypertension. ■

High Salt Intake Raises BP More In Metabolic Syndrome Patients



Source: Dr. Cubeddu

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Salsalate May Improve Metabolic Outlook in Obese Nondiabetics

BY DIANA MAHONEY
New England Bureau

BOSTON — Oral salsalate taken daily can reduce systemic inflammation and improve metabolic parameters in obese, nondiabetic adults, suggesting that it "may provide a novel therapeutic route for diabetes prevention," said Dr. Amy Fleischman at the annual meeting of the Endocrine Society.

Previous studies have shown that high-dose aspirin inhibits the inhibitory kappa B kinases/nuclear factor kappa B pathway, which is known to influence inflammation, and chronic, subacute inflammation is thought to play a role in the development of insulin resistance, type 2 diabetes, and cardiovascular disease. Salicylates have also been shown to improve glucose metabolism in patients with type 2 diabetes. Although high-dose aspirin therapy is not considered a safe option for diabetes prevention in at-risk populations because of the associated bleeding risks, salsalate, a nonacetylated dimer of salicylate, "is a much weaker inhibitor of cyclooxygenase enzymes, and as such, is clinically safer," said Dr. Fleischman of the Joslin Diabetes Center in Boston.

Dr. Fleischman and her colleagues conducted a double-blind, placebo-controlled trial of 20 nondiabetic individuals with a mean body mass index of 38 kg/m^2 and a mean age of 24 years; half were randomized to receive 4 g daily of salsalate and half were randomized to placebo.

At 1 month, the patients taking salsalate experienced a significant 8% reduction from baseline in fasting blood glucose values. Those who received placebo had a simultaneous increase in fasting blood glucose of 4% during that time. The glycemic response to glucose load, examined by oral glucose tolerance testing, improved on salsalate treatment, and worsened on placebo during the 1-month study. The glucose area under the curve improved significantly by 14% after 1 month of treatment.

Insulin levels in both study groups were unchanged, "but fasting and OGTT [oral glucose tolerance test] C-peptide levels were lower in the salsalate-treated subjects, which is consistent with what we know about salicylate's ability to inhibit insulin clearance," she said.

Homeostasis model assessment insulin resistance calculations showed significant improvement in insulin sensitivity in patients in the salsalate group, said Dr. Fleischman, adding that "circulating inflammatory markers responded to treatment." Specifically, mean fasting nonesterified fatty acid decreased 44%, mean C-reactive protein decreased 37%, and concentration the atheroprotective protein adiponectin increased 56%.

Salsalate treatment was generally well tolerated. Two patients in the active treatment group and one in the control group required dose reductions from 4 g to 3-3.5 g per day. At 1 month, mean salicylate levels were 17 mg/dL in the treatment group—similar to the blood salicylate levels seen with high-dose aspirin therapy. Creatinine and aspartate transaminase did not change in either group, indicating there were no toxic effects associated with salsalate therapy.

The findings also suggest that salsalate safely and effectively interferes with that inflammatory activity and by so, doing may be decrease an individual's risk of developing type 2 diabetes and cardiovascular disease, said Dr. Fleischman.

Salsalate is Food and Drug Administration approved for relief of signs and symptoms of osteoarthritis, rheumatoid arthritis, and other rheumatic diseases.

Dr. Fleischman disclosed no conflicts of interest related to her presentation. ■

Insulin Resistance in Normal-Weight Black Women Tied to Race

BY DIANA MAHONEY
New England Bureau

BOSTON — Normal-weight African American women were twice as likely to have insulin resistance as were similarly lean white and Hispanic women, based on the findings of an epidemiologic study.

In addition, unlike their white and Hispanic counterparts, African American women's increasing body mass index levels only minimally influenced their prevalence rate of insulin resistance, Dr. Jennifer Wolfgang said at the annual meeting of the Endocrine Society.

Race "may be an important independent risk factor for insulin resistance and potentially type 2 diabetes and heart disease," said Dr. Wolfgang of Wake Forest University, Winston-Salem, N.C. Weight-based screening standards may need to be adjusted so that even lean African American women are evaluated for insulin resistance, diabetes, and cardiovascular disease.

Dr. Wolfgang and her colleagues reviewed the data for participants in the multicenter Insulin Resistance Atherosclerosis Study, which was designed to evaluate the relationships between the degree of insulin sensitivity and variables associated with cardiovascular disease.

The approximately 1,600 men and women—all of whom were in general good health and without diabetes or impaired glucose tolerance—were divided by sex and placed into quartiles according to body mass index (BMI): less than 25, 25-30, 30-35, and greater than 35 kg/m^2. Among women in the lowest quartile, which is considered normal weight, 47% of the African Americans had insulin resistance (measured using the frequently sampled intravenous glucose tolerance test with minimal model analysis), compared with 18% of the whites and 15% of the Hispanics who were in this weight category.

After correction for age and recruitment sites, the difference in prevalence rates for African Americans, compared with whites and Hispanics, remained statistically significant, Dr. Wolfgang said. For the other three quartiles, the women had similar risk for insulin resistance across all three ethnic groups.

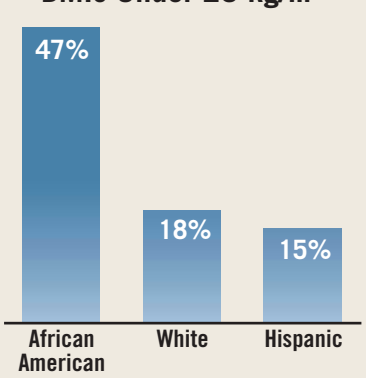
A similar trend was observed for African American men, but the differences were not statistically significant.

Dr. Wolfgang speculated that the ethnic disparities might be a consequence of between-race differences in the percentage or distribution of intraabdominal fat. Some yet-to-be-identified genetic variation also could be the source of the differences, she noted.

There is no simple clinical method for routinely measuring insulin resistance, Dr. Wolfgang acknowledged, but the observation of insulin resistance at low BMI levels in African American women argues for aggressive management of the more easily measured cardiovascular risk factors, such as high blood pressure, high cholesterol levels, and high blood glucose values.

Dr. Wolfgang reported no conflict of interest with respect to her presentation. ■

Rate of Insulin Resistance in Women With BMIs Under 25 kg/m^2



Note: Based on a study of 1,625 subjects.
Source: Dr. Wolfgang

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