

Intensive BP Therapy Cut Fracture Risk in ACCORD

Reduced risk may be a result of greater use of thiazides intensive group, high BMI of cohort.

BY RICHARD M. KIRKNER

FROM THE ANNUAL MEETING OF THE AMERICAN SOCIETY OF HYPERTENSION

NEW YORK – Intensive therapy to control systolic blood pressure did not appear to be associated with more falls and fractures in a study of patients under age 80 years with hypertension and type 2 diabetes, based on an analysis presented at the meeting.

The finding was noted in a sub-

Systolic blood pressure averaged 133 mm Hg in the standard treatment group and 119 mm Hg in the intensive treatment group. Subjects' average age was 62 years, and patients over age 80 years were excluded; 44% were women; 66% were white, 26% were black, and 2% Latino. Patients' average body mass index was 32.5 kg/m².

With an average follow-up of almost 5 years, ACCORD-BONE study results bucked conventional wisdom

about risk of falls, according to Dr. Margolis. "About 20% in the intensive group and 21% in the standard group fell," she said. The intensive group had a 0.81 relative risk of falling, compared with the standard group. The study found no differences across age, sex, ethnicity, or status of baseline diabetes.

The overall rate of self-reported falls was 70/100 person-years, Dr. Margolis said. "This also was lower in the intensive group at 62/100 person-years vs. the standard group at 74/100.

"With regard to nonspinal fractures, the study identified 273 individuals with at least one fracture, including 63 ankle, 34 humerus, 29 foot, 25 wrist, and 19 hip," said Dr. Margolis. "Overall, fracture risk was significantly lower in the intensive vs. the standard blood pressure group with a hazard ratio of 0.78," she said.

Dr. Margolis acknowledged the ACCORD-BONE study had some limits. "One of the most striking findings from the blood pressure treatment data was that there was a very, very large difference in thiazide use – thiazides being known to improve bone density – so that's a very suggestive mechanism," she said.

Dr. Joseph L. Izzo of the University of Buffalo, N.Y., remarked about obesity in the study group, noting the high average body mass index.

"I'm not sure that overweight people aren't protected in some way against blood pressure-related falls," Dr. Izzo said.

Physical activity might also explain why those on intensive therapy were less prone to falls and fractures, noted Dr. Bryan Williams of the University of Leicester, England. "To some extent falls are not always due to just people getting possible hypotension; they're related to amount of activity," he said.

Dr. Margolis said that a substudy would further investigate physical activity in this population. ■

VITALS

Major Finding: In older patients with type 2 diabetes, intensive blood pressure therapy significantly reduced the risk of fracture, compared with standard therapy (hazard ratio 0.78), but not the risk of falls (HR, 0.81).

Data Source: A subgroup analysis of 3,282 ACCORD-BONE participants in the ACCORD Blood Pressure Clinical Trial arm of ACCORD.

Disclosures: The National Heart, Lung, and Blood Institute and National Institute of Diabetes and Digestive and Kidney Diseases funded the ACCORD-BONE study. Dr. Margolis had no other disclosures to report.

group analysis of ACCORD-BONE, an ancillary study of skeletal health in ACCORD study participants. The subgroup analysis looked at ACCORD-BONE participants in the ACCORD Blood Pressure Clinical Trial arm of ACCORD, which showed that treating patients to a blood pressure target of less than 130/80 mm Hg offered no more protection against cardiovascular events than did treating them to a goal of less than 140 mm Hg.

For the subgroup analysis, the researchers examined data from 3,282 people who were randomly assigned to standard systolic blood pressure goals of 130-139 mm Hg or to intensive systolic goals of less than 120 mm Hg.

"Intensive control of systolic blood pressure did not result in an increased risk of falls," reported Dr. Karen Margolis of the Health Partners Research Foundation in Minneapolis. "And fewer intensive than standard group patients developed nonspinal fractures."

Average blood pressure at entry was 138/75 mm Hg. Those in the intensive therapy group received a thiazide-type diuretic in combination with another class of antihypertensive drug to a goal of 120 mm Hg. The standard intervention group used the same drugs and combinations, but the systolic goal was 130-135 mm Hg and treatment was only intensified if systolic blood pressure rose above 160 mm Hg, according to Dr. Margolis.

Broken Skin Barrier May Increase Type 2 Diabetes Risk

BY BRUCE JANCIN

FROM THE WORLD CONGRESS OF DERMATOLOGY

SEOUL, KOREA – Defective skin barrier function, as evidenced by common filaggrin mutations, may predispose patients to type 2 diabetes, according to the results of a Danish cross-sectional study.

Adult patients in the Danish general population who reported having diabetes had a significantly higher prevalence of filaggrin null mutations than did patients without diabetes. A confirmatory subgroup analysis conducted in a separate group of Danish patients known to have diabetes showed the same results, Dr. Jacob P. Thyssen reported.

This was a cross-sectional study, said Dr. Thyssen. As such, it doesn't establish causality. They are hypothesis-generating analyses – and the hypothesis they support is that a defective skin barrier allowing ready entry of allergens, chemical irritants, and microorganisms could increase the propensity for development of low-grade inflammation beyond the skin, including perhaps inflammation of the pancreas, with resultant type 2 diabetes, explained Dr. Thyssen of the National Allergy Research Center at Copenhagen University Hospital.

He and his colleagues came up with the hypothesis as a result of a recent study by other investigators who reported the existence of a specific subtype of asthma driven by filaggrin-defect-associated skin barrier dysfunction rather than sensitization (*Pediatr. Allergy Immunol.* 2010;21:954-61).

There is no filaggrin in the lung. So if deficient filaggrin expression in the outermost layer of the skin increases the likelihood of asthma, it may result in low-grade inflammation of the pancreas and type 2 diabetes, Dr. Thyssen hypothesized.

Filaggrin proteins cause keratin filaments in the epidermis to aggregate in ways that prevent epidermal water loss and impede entry of unwanted environmental chemicals, haptens, and proteins. Loss of filaggrin expression is strongly associated with atopic dermatitis.

Dr. Thyssen reported on a random sample of 3,335 adults drawn from the general Danish population, all of whom underwent genotyping for the two most common filaggrin mutations: R501X and 2282del4 null mutations.

Among this group were 133 individuals with self-reported diabetes and 66 others with screen-detected diabetes (*BMJ* 15 March 2011 doi: 10.1136/bmjopen-2011-000062).

The prevalence of the filaggrin mutations was 7.8% in the 3,136 subjects without diabetes, 12.8% in those with self-reported diabetes, and 9.1% in individuals

VITALS

Major Finding: Filaggrin mutations were found in 7.8% of nondiabetic patients, 6.7% of type 1, and 9.8% of type 2 patients.

Data Source: A random sample of 3,335 Danish adults.

Disclosures: Study was funded by the Danish government. Dr. Thyssen reported no financial conflicts.

who screened positive for diabetes.

Then, the investigators compared filaggrin mutation rates in the 3,136 patients without diabetes to those in 104 other patients with type 1 diabetes and 774 with type 2 diabetes.

The prevalence of filaggrin mutations was 7.8% in the patients without diabetes, 6.7% in those known to have type 1 diabetes, and 9.8% in those with type 2 diabetes.

At least three studies have reported an inverse association between type 1 diabetes and atopic dermatitis, and since atopic dermatitis is associated with an

increased prevalence of filaggrin mutations, it was to be expected that the patients with type 1 diabetes would have a relatively low prevalence of filaggrin mutations.

The link between filaggrin mutations and type 2 diabetes was dependent upon body mass index.

DR. THYSSEN



A logistic regression analysis showed the link between filaggrin mutations and type 2 diabetes was dependent upon body mass index. Patients with a BMI less than 25 kg/m² and filaggrin mutations were 2.1-fold more likely to have diabetes than those without filaggrin mutations. Among patients with a BMI of 25-30 kg/m², the odds of diabetes in patients with filaggrin mutations were 1.5-fold greater than in those with normal filaggrin, and in those with a BMI greater than 30 kg/m² there was no significant association between filaggrin and diabetes.

These results suggest that in obese individuals, other factors dwarf any impact filaggrin genotype may have over the development of diabetes, according to Dr. Thyssen.

This study raises the possibility that the documented prevalence trends for atopic dermatitis and type 2 diabetes are related through a defective skin barrier allowing penetration of allergens and chemicals that promote low-grade inflammation, he said. Another possibility deserving further consideration is whether the repeated course of topical and oral corticosteroids commonly used in the treatment of moderate-to-severe atopic dermatitis increases the risk of type 2 diabetes.

Dr. Thyssen stressed that his study requires confirmation. He and his colleagues are planning a 30-year follow-up study in the general Danish population. ■