

# Maximize Stroke Risk Reduction in Elderly

## Studies show benefits of calcium channel blockers and diuretics.

BY BRUCE JANCIN

EXPERT ANALYSIS FROM THE ANNUAL MEETING OF THE AMERICAN COLLEGE OF CARDIOLOGY

NEW ORLEANS – Calcium channel blockers and diuretics are the best drugs for treating hypertension in the elderly because they are the most effective at reducing the risk of what elderly patients fear most: stroke, Dr. Norman M. Kaplan asserted at the meeting.

“Coronary disease remains by far the most common cause of mortality [in the United States], but stroke poses the greatest threat to the elderly, not coronary disease,” said Dr. Kaplan, professor of internal medicine at the University of Texas, Dallas.

He presented a state-of-the-art perspective on antihypertensive therapy in the elderly from the unique vantage point of having served as a member of the third, fourth, fifth, and sixth Joint National Committees on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure.

Dr. Kaplan noted that a British meta-analysis of 46 randomized trials comparing each of the five major classes of antihypertensive drugs with any other class showed that all of the classes were similarly effective in preventing both coronary disease events and strokes, with one exception: calcium channel blockers had a significantly greater preventive effect on stroke than other agents. Diuretics showed a trend in the same direction that did not reach statistical significance (BMJ 2009;338:b1665 [doi:10.1136/BMJ.b1665]).

A secondary analysis of the 19,257-subject ASCOT (Anglo-Scandinavian Cardiac Outcomes Trial) demonstrated that calcium channel blocker-based antihypertensive

therapy was particularly effective against stroke in the population most in need of such protection: the elderly. Although there was no significant difference in strokes between amlodipine- and atenolol-based therapy in patients younger than age 65 years, there was a highly significant 30% relative risk reduction with amlodipine in the over-65 group (J. Hypertens. 2011;29:583-91).

The latest thinking regarding mechanism of benefit is that calcium channel blockers and diuretics are more effective at reducing stroke risk because they decrease within-individual variation in systolic blood pressure, unlike ACE inhibitors, angiotensin receptor blockers, and beta-blockers, all of which significantly increase it. In a meta-analysis of 389 randomized, controlled trials of antihypertensive therapy, stroke risk proved strongly related to this interindividual variation in blood pressure (Lancet 2010;375:906-15).

Calcium channel blockers may also have a neuroprotective effect. A French study of 378 elderly, nondemented, hypertensive patients with the complaint of memory loss showed that memory scores were significantly better in those on a calcium channel blocker than on any other class of antihypertensive medication (J. Hypertens. 2010;28:2485-93). Although that’s an intriguing finding, this was an observational study and needs confirmation, in Dr. Kaplan’s view.

Elderly hypertensives predominantly have isolated systolic hypertension. Because of the extensive body of evidence showing that such patients have a good response rate to diuretic monotherapy, he recommends using a diuretic as the first-line drug.

“I would start chlorthalidone – now having a resurgence as the diuretic of choice – at 12.5 mg/day, and add a calcium channel blocker if additional therapy is needed to reach 150/70 mm Hg, which I think is a rational goal to aim for in the elderly,” he said.

Indeed, although the 7th Joint National Committee

calls 140 mm Hg the upper limit of normal systolic blood pressure at all ages, nearly all the randomized trials that have shown a protective value for antihypertensive therapy in the elderly enrolled patients with a baseline systolic pressure in excess of 160 mm Hg, and achieved an on-treatment systolic pressure in the 150s or 160s.

“I do not think the evidence we have to date shows protective value for treatment in patients with a baseline systolic blood pressure below 160 mm Hg. There is evidence to suggest that if we lower the elderly patient’s systolic blood pressure more than 10-15 mm Hg, we may be invoking additional trouble rather than protecting the patient,” said Dr. Kaplan.

“These are old people who obviously have atherosclerotic vascular disease, even if they don’t show it. Reduction in diastolic blood pressure to 65 mm Hg or lower may reduce their coronary perfusion – which occurs only during diastole – to a degree that could invoke a cardiovascular catastrophe,” he continued.

Other important aspects of treating elderly hypertensive patients include identifying and overcoming postural hypotension, encouraging the consumption of one or two alcoholic drinks per day for the well-documented health benefits, starting a statin, and measuring home blood pressures to ensure that an individual really is being treated adequately, Dr. Kaplan said.

The risks posed by orthostatic hypotension were highlighted in a study of 374 unselected ambulatory adults with an average age of 70 years and no known cardiovascular disease or other comorbidities. An orthostatic decrease in systolic blood pressure greater than 20 mm Hg was present 2 minutes after standing in 12% of them. Over roughly 1 year of follow-up, cardiovascular events were 2.4-fold more frequent in that patient subset (Hypertension 2010;56:56-61).

Dr. Kaplan disclosed that he is on the speakers bureaus for Pfizer, AstraZeneca, Merck, Novartis, and Bayer. ■

# Moderate Hypertension Linked to Adverse Brain Changes

BY MITCHEL L. ZOLER

FROM THE ANNUAL MEETING OF THE AMERICAN COLLEGE OF CARDIOLOGY

NEW ORLEANS – Elderly people with modestly elevated systolic blood pressures showed significant declines in their mobility and cognition, and concurrent significant increases in brain damage, during 2 years of follow-up in a small study.

These correlations suggest a possible new reason to control blood pressure in the elderly, Dr. William B. White said at the meeting.

“These data support an interventional trial evaluating different thresholds of ambulatory systolic blood pressure for preventing white matter progression and functional decline in older people,” said Dr. White, professor of medicine and chief of the division of hypertension and clinical pharmacology at the University of Connecticut in Farmington.

He plans to compare target systolic blood pressures of 145 and 130 mm Hg, he said in an interview. “If you can intervene in patients with early-onset white matter disease and prevent progression, then you will do these people a big favor. I don’t think we will see regression [of white matter damage], just prevention of it getting worse. This is the first study I know of to longitudinally compare ambulatory blood pressure

with both white matter hyperintensity and functional decline in older people. Blood pressure turned out to be the most important” determinant of de-

phologic and physiologic dysfunction. Many patients diagnosed with Alzheimer’s disease probably had poorly controlled hypertension over their lifetime.”

Dr. White and his associates enrolled 72 people aged 75-89 with various degrees of mobility and cognitive impairment who underwent blood pressure, cognitive, mobility, and MRI brain assessments at entry and 24 months later. At baseline, their age averaged 82 years, their 24-hour ambulatory blood pressure averaged 126/66 mm Hg, and their average amount of brain white matter hyperintensity, a marker of brain damage, was 1% of their total brain volume. Two years later, their average ambulatory blood pressure stood at 131/67 mm Hg.

At both times, about 70% of patients received antihypertensive medication.

When the researchers compared the findings at the two measurement times, they found that for each 1% increase in the volume of white matter hyperintensity, subjects showed an average 0.31-second decrease in their walk time and a 33-millisecond increase in their simple reaction time on cognitive testing. In addition, for each 1-mm Hg increase in 24-hour systolic blood pressure over the 2-year period be-

tween measurements, the subjects had an average 0.04% increase in their volume of white matter hypertrophy.

In a different analysis, Dr. White and his associates divided the 72 people into tertiles based on their 24-hour systolic



**Blood pressure was the most important determinant of declines in cognition and mobility.**

DR. WHITE

blood pressure at their 2-year assessment. The top and bottom tertiles had average systolic pressures of 144 and 117 mm Hg. The top tertile showed a significantly larger increase in white matter hyperintensity volume over the 2 years of follow-up, a significantly longer 8-foot walk time, a significantly slower walking speed, and nonsignificant trend toward poorer results on cognition tests.

Also notable in the findings was that a modest level of systolic hypertension in the highest tertile linked with significant changes over the 2-year period. “The people only averaged 144 mm Hg. That’s not so bad, but they had progression,” Dr. White said. ■

VITALS

**Major Finding:** A significant correlation was found between 24-hour ambulatory systolic hypertension, brain damage, and functional and cognitive impairment in elderly people. Each 1-mm Hg rise in systolic pressure over a 2-year period linked with an average 0.04% increased brain volume of white matter hyperintensity.

**Data Source:** Two-year follow-up study of 72 people aged 75-89 years (average age, 82 at baseline) who were normotensive or mildly hypertensive at entry.

**Disclosures:** Dr. White said that he has been a consultant to the Forest Research Institute and has received research grants from Novartis.

clines in cognition and mobility and in an MRI measure of brain damage, “and blood pressure is something where we can intervene,” he said.

“Hypertension specialists think about the burden [of hypertension] on the heart and the kidney, but they don’t think about the chronic burden on the brain,” said Dr. C. Venkata S. Ram, professor of medicine at the University of Texas Southwestern Medical Center in Dallas. “Chronic hypertension can lead to significant mor-