

Aldosterone Antagonists Treat Tough HT

Striking Odds

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BY MITCHEL L. ZOLER
Philadelphia Bureau

NEW YORK — Evidence is accumulating that an aldosterone antagonist can be a safe and effective treatment for patients with refractory hypertension that has not responded to one or more agents from the first-line antihypertensive drug classes.

Study results further show that aldosterone antagonists, specifically spironolactone and eplerenone, have a range of beneficial effects for patients with hypertension-related cardiovascular disease, including improved heart failure, reduced left ventricular size, improved endothelial function, reduced proteinuria and preserved renal function, and a reduced stroke risk, Dr. David A. Calhoun said at the annual meeting of the American Society of Hypertension.

"Treatment with either eplerenone or spironolactone leads to a substantial reduction in blood pressure when given as monotherapy. The big question for treating primary hypertension is how to use this class of drugs. They are not first-line agents yet," said Dr. Calhoun, a physician and hypertension specialist at the University of Alabama, Birmingham. He is a consultant to Pfizer Inc., which markets eplerenone (Inspra). Spironolactone is a generic drug.

Dr. Calhoun said that in his experience, a dangerously elevated serum level of potassium usually does not occur in patients treated with one of these drugs. Hyperkalemia is generally defined as a serum potassium level that reaches or exceeds 5.5 mEq/L.

"As long as patients' renal function is good, they're usually okay," he said.

The value of an aldosterone antago-

nist for lowering pressure in patients with refractory hypertension was documented in a poster at the meeting from researchers at Rush University in Chicago. They reported on a series of 27 patients who were treated with either 12.5 or 25 mg/day spironolactone, or 50 mg/day eplerenone. These 27 patients were identified as aldosterone-antagonist recipients from among 1,034 patients who had been treated by a hypertension specialist at Rush. All 27 patients were treated with an aldosterone antagonist because their pressure remained above their goal despite treatment with at least three other medications, and an average of more than five drugs per patient.

When their pressures were measured 3-6 weeks after starting their new regimen (average of 35 days), their systolic pressure had dropped from an average of 151 mm Hg before adding the aldosterone antagonist to an average of 144 mm Hg after, a statistically significant difference, reported Dr. Nitin Khosla, a physician at Rush, and his associates. Diastolic pressure fell by an average of 3 mm Hg, not a statistically significant difference.

None of the 27 patients developed hyperkalemia. Their average serum potassium level was 3.9 mEq/L before the new regimen began and 4.4 mEq/L after.

Results reported in a second poster at the meeting documented the efficacy of aldosterone antagonists for lowering blood pressure in patients with chronic kidney disease, defined as an estimated glomerular filtration rate of less than 30 mL/min.

Medical records were reviewed for 836

patients with chronic kidney disease who were treated by any of 10 nephrologists at St. John Hospital in Detroit beginning in 2004. Sixty-nine of the patients were treated with an aldosterone antagonist as part of their multidrug, blood pressure-lowering regimen. Most patients received three to five antihypertensive drugs. The most commonly used drug class was the loop diuretics, which were prescribed to 535 patients, followed by the β -blockers, used on 513 of the patients.

In an analysis that assessed the prevalence of blood pressure control by each drug class used, aldosterone antagonists were the second-most-effective class; about 58% of patients who received an aldosterone antagonist reached their goal blood pressure, exceeded only by the group that received a diuretic other than a loop or thiazide agent, which was linked with a 70% control rate, reported Dr. Joel M. Topf, a clinical nephrologist at St. John Hospital, and his associates.

Among patients with stage 4 or 5 kidney disease, treatment with an aldosterone antagonist was associated with the highest rate of blood pressure control, in 70% of patients. Treatment with an aldosterone antagonist was associated with a "surprisingly high rate of blood pressure control," the researchers stated in their poster.

The average serum potassium level in patients treated with an aldosterone antagonist was 4.55 mmol/L. The highest average serum potassium level was in the patients treated with an angiotensin-receptor blocker or an ACE inhibitor. Patients who got one of these drugs had an average serum potassium level of 4.71 mmol/L. ■

in their records; patients with type 1 diabetes were excluded. The study also included 1,219,047 people without type 2 diabetes. Overall, hypertension was diagnosed in 63% of patients with type 2 diabetes, compared with 40% of those without.

The difference was striking among children younger than age 12 years. Essential hypertension was present in 26% of the 219 with type 2 diabetes, compared with just 0.5% of the 49,984 without, for an unadjusted odds ratio of 56.1.

Even after adjustment for age, gender, geographic region, and five comorbid conditions (obesity, hyperlipidemia, nephritis, ischemic heart disease, and other forms of heart disease), children aged 0-11 years with type 2 diabetes still were more than 20 times more likely than those without to have essential hypertension, Dr. Jacober and his colleagues reported. Among adolescents aged 12-19 years, essential hypertension was present in 9.7% of the 691 with type 2 diabetes vs. 1.8% of the 61,129 without. In this age group, the unadjusted odds ratio was 4.4 and the adjusted odds ratio was 2.3, also highly significant.

Differences were less dramatic among adults, but still were significant for all age groups even after adjustment. Among the 2,808 young adults aged 20-29, essential hypertension was present in 21% of those with type 2 diabetes vs. 7% of those without.

The prevalence of essential hypertension among the diabetics increased by decade of life from 36% at ages 30-39 to 70% at ages 70-79, dropping to 67% among people over 80 years of age. Among the nondiabetics, essential hypertension was present in 20% of the 30-39 year olds, rising to 60% for those aged 70-79, and again dropping slightly thereafter to 58%. ■

Pilot Study Shows Spinal Realignment Improves Systolic Hypertension

BY MITCHEL L. ZOLER
Philadelphia Bureau

NEW YORK — Spinal manipulation reduced the systolic pressure in selected patients with hypertension in a controlled pilot study with 50 patients.

Realignment of the atlas vertebra seemed to lower the systolic blood pressure of 25 patients during 8 weeks of follow-up without drug therapy. A control group of 25 patients who underwent a mock realignment had no reduction in their systolic pressure, Dr. George L. Bakris and his associates reported in a poster at the annual meeting of the American Society of Hypertension.

Anatomical abnormalities of the cervical spine at the level of the atlas vertebra are associated with relative ischemia of the brainstem circulation and increased blood pressure. Impaired blood supply to the brain may affect the sympa-

thetic nervous system and sympathetic tone, said Dr. Bakris, professor of preventive medicine and director of the Hypertension/Clinical Research Center at Rush University in Chicago.

The pilot study enrolled patients with stage 1 hypertension who had no neck pain and evidence of atlas misalignment on preliminary screening. The patients were either withdrawn from their antihypertensive medications or had been treatment naive at entry to the study.

The atlas realignment procedure used was the standard treatment of the National Upper Cervical Chiropractic Association. Briefly, the patient's head is placed on a curved, mastoid support, which acts as a fulcrum. The patient's nondominant hand is positioned around the dominant wrist, and then the dominant hand is placed on a "corner" of the atlas's transverse process. External nudges are

used to cause the atlas vertebra to recoil into a normal alignment.

The control patients underwent a sham procedure designed so that correct alignment wasn't achieved.

At baseline, average systolic blood pressure was 150 mm Hg in the control patients and 147 mm Hg in the patients who then underwent a realignment procedure.

The average systolic pressure of the actively treated patients began to show a statistically significant drop relative to the control patients at 3 weeks after treatment, and their systolic pressure steadily declined during the following 5 weeks. By 8 weeks after treatment, the average systolic pressure in the treated group was less than 130 mm Hg. By contrast, the control group had no drop in average systolic pressure throughout follow-up. At 8 weeks after their sham procedure, the average systolic pressure was unchanged, at about 148 mm Hg. ■

Aldosterone May Aggravate Sleep Apnea in Hypertensives

NEW YORK — A link between aldosterone, hypertension, and obstructive sleep apnea was established in a study with 71 patients.

"We found an extraordinarily high prevalence of obstructive sleep apnea in patients with [treatment-] resistant hypertension," and serum aldosterone levels were significantly related to the severity of sleep apnea," Dr. David A. Calhoun said at the annual meeting of the American Society of Hypertension.

"We went in thinking that obstructive sleep apnea was driving aldosterone release, but now we think that a high serum level of aldosterone somehow contributes to worsening sleep apnea," said Dr. Calhoun, a hypertension specialist at the University of Alabama, Birmingham. The link may be mediated by increased salt and water retention or by

a change in flow resistance.

The current study involved a consecutive series of 41 men and 30 women who were referred to the hypertension clinic at UAB because of treatment-resistant hypertension. Their mean blood pressure was 156/88 mm Hg despite treatment with an average of four antihypertensive drugs.

The patients were assessed for obstructive sleep apnea by diagnostic polysomnography. The overall prevalence of obstructive sleep apnea was 85%, with a prevalence of 90% in the men and 79% in the women.

The average apnea-hypopnea index for all patients was 24 apnea events per hour.

The patients with sleep apnea also had high serum and urine levels of aldosterone. Patients with the most severe sleep apnea had the highest levels, Dr. Calhoun said.

—Mitchel L. Zoler