

# Findings Put New Spin On HT Combo Therapy

BY BRUCE JANCIN  
Denver Bureau

ORLANDO, FLA. — Combination anti-hypertensive therapy with a calcium channel blocker and angiotensin-converting enzyme inhibitor provides important clinical outcome advantages over the traditional  $\beta$ -blocker/diuretic combination, Peter S. Sever, Ph.D., said at the annual meeting of the American College of Cardiology.

He reported on 19,257 hypertensive patients free of coronary heart disease (CHD) who participated in the Anglo-Scandinavian Cardiac Outcomes Trial Blood Pressure-Lowering Arm (ASCOT-BPLA) who were randomized to amlodipine/perindopril or atenolol/bendroflumethiazide.

The study was halted early, after a mean 5.4 years, because of a highly significant 14% reduction in the relative risk of all-cause mortality that favored the group administered amlodipine/perindopril.

Preliminary ASCOT results indicate that at the 5-year mark, 1,178 cardiovascular events and procedures had occurred in the amlodipine/perindopril group, compared with 1,376 in the atenolol/bendroflumethiazide arm, said Dr. Sever, professor of clinical pharmacology and therapeutics at Imperial College, London.

Other significant differences in study end points—all of which favored the calcium channel blocker/ACE inhibitor combination—were included:

- ▶ A 32% reduction in new-onset diabetes.
- ▶ A 23% decrease in the incidence of fatal and nonfatal stroke.
- ▶ A 24% drop in cardiovascular mortality.
- ▶ More favorable HDL and triglyceride levels.

Blood pressures were an average of 2.9/1.8 mm Hg lower in the amlodipine/perindopril group. But that's sufficient to account for only part of the observed benefit, according to Dr. Sever. Additional possible explanations include a suspected adverse interaction between atenolol/bendroflumethiazide and statin therapy, and more effective inhibition of the renin-angiotensin system by amlodipine/perindopril.

**All study end points favored combined use of a calcium channel blocker and an ACE inhibitor.**

DR. SEVER

Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure VII guidelines recommending thiazide diuretics and  $\beta$ -blockers as initial treatment.

Discussant Richard Devereux, M.D., professor of medicine at Cornell University in New York, noted that the traditional  $\beta$ -blocker/diuretic combination was certainly not placebo therapy. These drugs are of long-established benefit in the treatment of hypertension. But the calcium channel blocker/ACE inhibitor combination was clearly superior.

Dr. Sever is a consultant to Pfizer Inc. and the Servier Research Group, the study's major sponsors. ■



# Nicardipine Safe for Cutting BP in Hypertensive Emergency

BY JANE SALODOF MACNEIL  
Southwest Bureau

PHOENIX, ARIZ. — Intravenous nicardipine can reduce blood pressure by 15%-20% without impairing blood supply to the brain in hypertensive emergencies, preliminary results from an ongoing case-control study suggest.

Results so far suggest nicardipine therapy might even improve cerebral oxygenation (PbrO<sub>2</sub>) in ischemic patients, reported study investigator Varun Puri, M.D. "There was no reduction in oxygen delivery to the brain despite significant reduction in [the fraction of inspired oxygen]," he said at a meeting sponsored by the Society of Critical Care Medicine.

Dr. Puri presented data on 17 patients with acute neurological disorders, 11 of whom were women. The patients' average age was 57 years, and the pathologies included seven subarachnoid hemorrhages, four traumatic brain injuries, three intracerebral hemorrhages, two arteriovenous malformations, and one case of anoxia.

The patients had 36 episodes of hypertensive emergency during the study: 11 from acute cardiovascular syndrome, 14 postoperatively, and 11 after trauma. The nicardipine dose, titrated as clinically indicated to lower blood pressure, ranged from 2.5 mg to 15 mg per hour. The duration of treatment ranged from 12 hours to 10 days.

Dr. Puri reported that systolic blood

pressure fell from 175 mm Hg pretreatment to 143 mm Hg at 8 hours after treatment, diastolic blood pressure decreased from 84 mm Hg to 69 mm Hg, and mean arterial blood pressure dropped from 114 mm Hg to 95 mm Hg. All the changes were statistically significant.

Brain tissue monitoring over an 8-hour period showed no significant changes in intracranial pressure or partial brain tissue oxygenation (PbtO<sub>2</sub>). Fraction of inspired oxygen (FiO<sub>2</sub>) fell from 0.72 to 0.62, a statistically significant difference.

In six patients presenting with cerebral hypoxia, average PbtO<sub>2</sub> was 10.4 mm Hg before treatment with nicardipine, a specific arterial dilator. By 4 hours posttreatment, oxygenation had increased to 20.4 mm Hg. At 8 hours, it was 22.2 mm Hg, a statistically significant change.

One severe adverse event was reported: a case of hypotension that responded quickly to a reduction in the nicardipine dose, Dr. Puri said. Five patients eventually required oral antihypertensive agents, and three went on to  $\beta$ -blockers, he said. None had been on  $\beta$ -blockers before the trial, and patients taking two or more agents for hypertension had also been excluded.

The investigators are continuing to enroll patients, said Dr. Puri, of Creighton University Medical Center in Omaha, Neb. Integra LifeSciences Corp., maker of the Licox brain tissue oxygen monitoring system, provided funding for the study. ■

# Meditation Benefits Black Teens With High-Normal BP

BY MIRIAM E. TUCKER  
Senior Writer

VANCOUVER, B.C. — Transcendental meditation may improve vascular function in African American teenagers with high-normal blood pressure, Vernon A. Barnes, Ph.D., said at the annual meeting of the American Psychosomatic Society.

Transcendental meditation (TM), a process by which "the mind is allowed to settle down to a state of least mental activity," has been shown to decrease sympathetic nervous system tone, hypothalamic-pituitary-adrenocortical axis activation, and cortisol levels, which are associated with reductions in blood pressure.

In a study by Dr. Barnes and his associates at the Medical College of Georgia, Augusta, systolic and diastolic blood pressures were significantly reduced in 50 African American adolescents with high-normal blood pressures who practiced TM twice a day for 4 months (*Am. J. Hypertens.* 2004;17:366-9).

In that study, 57 African American adolescents (mean age 16.2 years) were randomized to practicing TM for 15 minutes, twice a day for 4 months. One session was

held in school during homeroom, the other was practiced at home. Another 54 teens received 15-minute didactic health education sessions about weight management, healthy diet, and physical activity each day at school, and also were assigned to walk 15 minutes a day.

At-home compliance with the meditation—in which "the ordinary thinking process becomes quiescent and a distinctive wakeful but deeply restful state" is achieved—was 76%, including weekends and holidays, Dr. Barnes told this newspaper.

Echocardiographic-derived measures of the subjects' endothelium-dependent vasodilation to reactive hyperemia (EDAD)—a functional measure of vascular remodeling that is inversely correlated with cardiac structure and function—were collected before and after the interventions, and again at 4 months' follow-up.

The procedure involved scanning the subjects' right brachial artery prior to and for 2 minutes following 4 minutes of hyperemia, which was induced by inflating the cuff to 200 mm Hg. EDAD was calculated as the percentage change from baseline diameter to maximum post-cuff

release diameter. The sonographer was blinded to which group the subject was in, Dr. Barnes said.

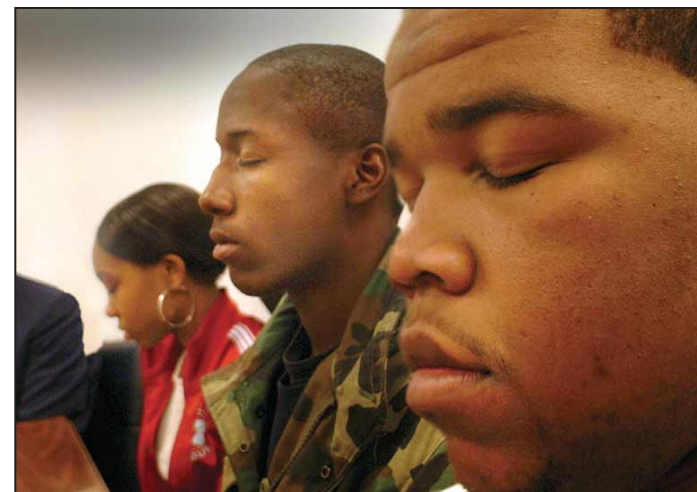
From pre- to 4 months post intervention, EDAD in the TM group increased by 21%, from 12.4% to 15%, compared with a 4% decrease of 12.3% to 11.8% in the health education group.

"If this improvement is replicated among other at-risk groups and in cohorts of cardiovascular disease patients, this will have important implications for inclusion of TM in the efforts to prevent and treat CVD and its clinical consequences," he said.

Other benefits were seen as well. Anecdotes related by the students corroborated school records documenting improved behavior related to school, fewer rule violations, and fewer

days suspended. Students also reported improvements in sleep, athletic and school performance, and personal relationships, Dr. Barnes said.

This study, which was funded by the National Heart, Lung, and Blood Institute, was singled out by the psychosomatic society as among those "having the highest potential to change clinical practice." ■



Teenagers who meditated for 15 minutes, twice a day for 4 months, had improvement in a measure of vascular remodeling.