Studies Bring New Focus to Hormone Therapy

A novel progestin with antialdosterone effects is being developed to help treat postmenopausal symptoms.

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ATLANTA — A new hormone therapy for postmenopausal symptoms also has a significant antihypertensive effect; the popular β-blocker carvedilol comes in a once-daily formulation; and an analysis of more than 600 representative patients with hypertension quantified the potential for reducing coronary heart disease by controlling blood pressure and serum lipids. These three poster reports were among the hypertension studies presented at the annual meeting of the American College of Cardiology.

New Progestin Lowers Blood Pressure

Drospirenone is a new progestin with antialdosterone effects that is being developed for use with 17-b estradiol to treat postmenopausal symptoms. The effect of drospirenone and estradiol on blood pressure was assessed in a dose-ranging study with 750 women. All participants were postmenopausal women with mild to moderate hypertension, with a systolic pressure of 140-179 mm Hg and a diastolic pressure of 90-109 mm Hg when off treatment.

The women were randomized to treatment with estradiol alone; estradiol plus 1 mg, 2 mg, or 3 mg of drospirenone daily; or placebo. After 8 weeks of treatment, average clinical blood pressure readings in the placebo group had fallen by 8.7 mm Hg (systolic) and by 5.0 mm Hg (diastolic), compared with baseline. Estradiol treatment alone produced no significant reduction in blood pressure, compared with the placebo effect.

Women treated with 1 mg of drospirenone daily had an average additional systolic blood pressure reduction of 0.9 mm Hg and an additional diastolic pressure reduction of 2.0 mm Hg, compared with the placebo group; this was of borderline statistical significance.

The higher dosages of drospirenone had a more marked effect. Women taking a 2-mg daily dosage had an average additional fall in systolic pressure of 3.4 mm Hg and in diastolic pressure of 4.0 mm Hg, compared with the placebo group, which were statistically significant declines, reported Dr. William B. White, chief of the section of hypertension and clinical pharmacology at the University of Connecticut, Farmington, and his associate. Similar drops in pressure were also seen in women who received 3 mg of drospirenone daily.

An estimated third to half of CHD events could be prevented by reductions in blood pressure and improved serum levels of LDL and HDL cholesterol.

All three dosages of drospirenone were "well tolerated, with modest subjective or objective adverse events," said Dr. White and his associate in their poster. The percentage of patients who developed hyperkalemia while on treatment was similar in all five treatment groups.

Other details of adverse effects were not reported. Further studies are needed to examine the effect of treatment for 2 or more years, he said. The study was sponsored by Berlex, which is developing drospirenone.

Once-Daily Carvedilol

Carvedilol is a widely used β-blocker that is effective for lowering blood pressure and is especially popular for treating patients with heart failure. The only available formulation of carvedilol requires twice-daily dosing. A placebo-controlled, dose-ranging study with a total of 338 patients was done to assess the blood pressure–lowering effects of a controlled-release (CR) once-daily formulation of carvedilol.

The study enrolled patients with diastolic blood pressures of 90-109 mm Hg. Patients were randomized to treatment with 20 mg, 40 mg, or 60 mg of carvedilol CR or placebo once daily for 6 weeks. The study's primary end point was the change in mean diastolic blood pressure, measured by ambulatory blood pressure monitoring, in the treatment groups, compared with those on placebo.

Placebo use led to an average 0.4–mm Hg decline in mean, 24-hour diastolic pressure. The three dosages of carvedilol CR led to significantly larger declines in a dose-dependent manner. The average falls in diastolic pressure were 4.4 mm Hg, 7.9 mm Hg, and 9.6 mm Hg in the 20-mg, 40-mg, and 60-mg groups, respectively, reported Dr. Michael A. Weber, professor of medicine at the State University of New York, Brooklyn, and his associates. Similar drops were also seen in systolic blood pressure. Blood pressure control was maintained for 20-24 hours after a dose of carvedilol CR.

The rates of adverse effects and of adverse effects leading to withdrawal from treatment were similar in all four treatment groups.

GlaxoSmithKline, which is developing carvedilol CR (Coreg CR), submitted a New Drug Application to the Food and Drug Administration last December to have carvedilol CR approved as a treatment for hypertension. Testing of carvedilol CR for treatment of patients with heart failure is ongoing.

CHD Linked to Hypertension, Lipids

In patients with hypertension, a third to a half of their coronary heart disease events could be prevented by reductions in their blood pressure and improved serum levels of LDL and HDL cholesterol. Three-quarters of their events could be prevented by optimal control of these three parameters, Dr. Nathan D. Wong and his associates reported in a poster.

They made these estimates by analyzing data collected for 1,921 people in the National Health and Nutrition Examination Survey (NHANES) 2001-2002. The study focused on the 676 people from this group who had hypertension, defined as a blood pressure of 90 mm Hg diastolic or 140 mm Hg systolic or greater, or a pressure of 80 mm Hg diastolic or 130 mm Hg systolic or greater in patients with diabetes.

Using the Framingham risk formula for the 10-year risk of coronary heart disease events, Dr. Wong and his associates calculated the projected number of events expected for these 676 people on the basis of their clinical characteristics at the time of the survey. The calculations also showed that more events would be prevented by combined control of blood pressure and serum lipids than by the additive effect of controlling each of these parameters alone, said Dr. Wong, director of the heart disease prevention program at the University of California, Irvine. The study was sponsored by Pfizer Inc. ■

Gender May Factor Into ICD Efficacy

ATLANTA — Women may not derive a significant mortality benefit from implantable cardioverter defibrillator therapy, Nickole N. Henyan, Pharm.D., said at the annual meeting of the American College of Cardiology.

She presented a metaanalysis examining gender's effect on all-cause mortality in the major randomized controlled trials of implantable cardioverter defibrillator (ICD) therapy for primary prevention of arrhythmic death.

The metaanalysis included five randomized trials totalling 6,405 subjects, 1,575 of them women. The five other major trials had to be excluded because they didn't break down the outcomes by gender, explained Dr. Henyan of the University of Connecticut School of Pharmacy, Storrs, and Hartford (Conn.) Hospital.

The risk of all-cause mortality in men who received an ICD was reduced by 26% relative to controls who got the then-standard therapy. In contrast, the relative risk reduction in women with an ICD was 19%, which didn't attain statistical significance.

Moreover, when the metaanalysis was redone with exclusion of the 1,520-patient Comparison of Medical Therapy, Pacing, and Defibrillation in Heart Failure (COMPANION) trial, on the grounds that COMPANION studied ICD therapy in combination with biventricular pacing, the gender disparity in all-cause mortality became even more pronounced. Men who got an ICD showed a highly significant 24% reduction in all-cause mortality compared with male controls, whereas women who received an ICD experienced only a nonsignificant 12% relative risk reduction.

"Perhaps we're overtreating women by implanting ICDs for primary prevention," Dr. Henyan said. "There are concerns of cosmetic alteration and inappropriate shocks that come with an ICD, and no patient should have to endure this unless significant life-saving benefit results."

Session moderator Dr. Douglas P. Zipes was skeptical.

"Those data are extremely provocative. To my knowledge, ventricular fibrillation is the same whether you're a man or a woman, and a shock should terminate it. I have no answer as to why there should be a gender difference to an ICD response, assuming patients are matched in terms of sickness and ejection fraction," said Dr. Zipes, distinguished emeritus professor of medicine at Indiana University, Indianapolis.

—Bruce Jancin

Acupuncture Therapy Cuts Mild Hypertension, but Not for Long

DALLAS — Acupuncture proved effective and safe for the treatment of mild to moderate hypertension in a randomized, single-blind German clinical trial.

This form of therapy may have appeal for a segment of the population that dislikes taking medication, but it's not curative; 3 months after completion of the course of acupuncture, blood pressures (BPs) were back at baseline levels, Dr. Frank A. Flachskampf reported at the annual scientific sessions of the American Heart Association.

The trial involved 160 patients aged 45-75 years with mild to moderate, uncomplicated arterial hypertension who were randomized to a 6-week course of traditional Chinese acupuncture or to sham acupuncture. Both regimens consisted of 22 sessions of 30 minutes' duration, delivered by extensively trained Chinese acupuncturists.

Overall, 78% of study participants were on antihypertensive medication at baseline, and their dosing remained unchanged during the trial.

There were 72 patients in the acupuncture arm and 69 assigned to sham acupuncture who completed the study. Mean 24-hour ambulatory BP in the acupuncture group fell from 131/81 mm Hg at baseline to 125/78 at the end of the 6-week program. In contrast, ambulatory BP remained unchanged in the sham-therapy group, according to Dr. Flachskampf of the University of Erlangen, Germany.

Follow-up 24-hour ambulatory BP monitoring conducted 3 and 6 months after completing the acupuncture showed BPs had returned to pretreatment levels.

Two patients in the acupuncture group dropped out of the study because they said acupuncture was too painful; they were the only subjects who reported any side effects.

—Bruce Jancin