Revisions Unveiled

Guidelines *from page 1*

Interventions for Atherosclerotic Disease

The writing committee recommended that patients with stenosis of the carotid artery or vertebral artery should receive optimal medical therapy, including antiplatelet drugs, statins, and risk factor modification. In patients whose TIA or stroke was due to 50%-99% stenosis of a major intracranial artery, they advised prescribing aspirin therapy (50-325 mg daily) over warfarin. Long-term maintenance of blood pressure at less than 140/90 mm Hg and total cholesterol at less than 200 mg/dL "may be reasonable," they wrote. The usefulness of angioplasty, with or without stent placement, for an intracranial artery stenosis is not yet known in this population and is considered investigational. Extracranial-intracranial bypass surgery is not recommended.

For patients with atherosclerotic ischemic stroke or TIA who do not have coronary heart disease, the committee stated that "it is reasonable to target a reduction of at least 50% in LDL-C or a target LDL-C level of less than 70 mg/dL."

Antithrombotics for Stroke

The guidelines recommend that patients who need anticoagulation therapy but cannot take oral anticoagulants should be given aspirin alone. They warn that the combination of aspirin plus clopidogrel "carries a risk of bleeding similar to that of warfarin and therefore is not recommended for patients with a hemorrhagic contraindication to warfarin."

Any temporary interruption to anticoagulation therapy in patients who have atrial fibrillation and are otherwise at high risk for stroke calls for the use of bridging therapy with subcutaneous administration of low-molecular-weight heparin, according to the guidelines.

Dr. Furie and the committee members recommended caution in using warfarin in patients who have cardiomyopathy characterized by systolic dysfunction (a left ventricular ejection fraction of 35% or less) because of a lack of proven benefit.

Evidence is also insufficient to establish whether anticoagulation therapy is better than aspirin therapy for secondary stroke prevention in patients who have a patent foramen ovale.

The guidelines also address secondary stroke prevention under a variety of special circumstances, such as cases of arterial dissection, hyperhomocysteinemia, hypercoagulable states, and sickle cell disease. They also detail management specific to women, particularly concerning pregnancy and the use of postmenopausal hormone therapy.

Dr. Furie reported receiving research grants from the National Institute of Neurological Disorders and Stroke as well as the ASA-Bugher Foundation Center for Stroke Prevention Research. Some of her 17 coauthors disclosed receiving research support from, being a speaker for, or consulting to or sitting on an advisory board for companies that manufacture drugs commonly prescribed for stroke prevention. ■

The guidelines can be obtained at www.americanheart.org/presenter.jhtml?identifier=3003999 or by calling 843-216-2533.

Intensive BP Control Didn't Shine in Chronic Kidney Disease

BY MARY ANN MOON

FROM THE NEW ENGLAND JOURNAL OF MEDICINE

Intensive blood pressure control didn't slow the progression of chronic kidney disease any better than standard blood pressure control in most patients, according to a report in the New England Journal of Medicine.

It appears that the more intensive approach may benefit only patients who have proteinuria with a protein-creatinine ratio greater than 0.22, a value that is compatible with the widely accepted threshold of 300 mg/day for absolute urinary protein excretion, said Dr. Lawrence J. Appel of Johns Hopkins University, Baltimore, and his associates in the AASK (African-American Study of Kidney Disease and Hypertension) Collaborative Research Group.

Until now, "few trials have tested the effects of intensive blood pressure control [compared with conventional control] on the progression of chronic kidney disease, and the findings from such trials have been inconsistent. Despite a lack of compelling evidence, numerous guidelines recommend a reduced blood pressure target in patients with [chronic kidney disease]," they wrote.

Previous studies have rarely followed patients beyond 5 years, even though it typically takes longer than that for end-stage renal disease (ESRD) to develop in patients with CKD, the researchers noted.

The AASK study compared outcomes between the two approaches to blood pressure control in 1,094 black adults with mild to moderate hypertensive chronic kidney disease (defined as diastolic BP greater than 95 mm Hg and a glomerular filtration rate of 20-65 mL/min) but without marked proteinuria.

Patients with diabetes were excluded from the clinical trial.

In the first phase of the AASK investigation, patients were randomly assigned to either intensive BP control with a target of 92 mm Hg or lower mean arterial pressure (that is, lower than the usual target of 130/80 mm Hg recommended for CKD patients) or to conventional BP control with a target of 102-107 mm Hg mean arterial pressure (which corresponds to the conventional BP target of 140/90 mm Hg).

Throughout this initial phase of the trial, which lasted approximately 4 years, mean blood pressure was significantly lower in the intensive-control group (130/78 mm Hg) than in the standard-control group (141/86 mm Hg).

However, there was no significant difference in the primary outcome of progression of kidney disease, development of ESRD, or death.

Likewise, there was no significant difference between the two approaches in secondary or clinical outcomes, the investigators noted.

In the second phase of the AASK investigation, patients who had not yet developed ESRD were invited to continue in a cohort portion of the trial, in which the BP target was 140/90 mm Hg.

In 2004, when national guidelines were changed, this target was amended to lower than 130/80 mm Hg.

After a cumulative follow-up of 8-12 years, there still was no significant difference in primary or secondary outcomes between those who were initially assigned to the intensive-control and the standard-control groups.

More intensive blood pressure control did not slow the rate of progression of CKD, Dr. Appel and his associates reported (N. Engl. J. Med. 2010;363: 918-29).

However, the intensive-control approach did benefit one subgroup of patients with proteinuria: those who had a protein-creatinine ratio of more than 0.22 at baseline, the study investigators said.

These patients showed a significant reduction in the primary outcome of progression of kidney disease, development of ESRD, or death, as well as in secondary and clinical outcomes, the researchers added.

The reason for this discrepancy is not known.

"Overall, it is hard to develop a coherent, biologically plausible argument for a qualitative interaction between harm in patients without proteinuria and benefit in those with proteinuria," the study authors said. ■

VITALS

Major Finding: Compared with standard BP control, intensive BP control failed to slow the progression of CKD, prevent the development of end-stage renal disease, or prevent death in most patients who had mild to moderate chronic kidney disease. Intensive BP control was beneficial only in the subgroup of patients who had proteinuria with a protein-creatinine ratio greater than 0.22 at baseline.

Data Source: AASK, a clinical trial with an initial 4-year randomized phase comparing intensive BP control with standard BP control in 1,094 black adults, as well as an observational cohort phase with a further 4-8 years of extended follow-up.

Disclosures: This study was funded by the National Institute of Diabetes and Digestive and Kidney Diseases, the Office of Research in Minority Health, and the National Institutes of Health. King Pharmaceuticals provided financial support and donated antihypertensive medications to each clinical center. AstraZeneca, GlaxoSmithKline, Forest Laboratories, Pharmacia, Pfizer, and Upjohn also donated antihypertensive drugs. None of these companies had any role in the design of the study, the accrual or analysis of data, or the preparation of the manuscript. Some of the investigators reported being in consultant and/or advisory board roles or receiving funds from numerous companies including Daiichi-Sankyo, Novartis, Amgen, King Pharmaceuticals, Abbott, Boehringer-Ingelheim, Litholink, Eli Lilly, Takeda, Merck, and Watson.

VIEW ON THE NEWS

Findings Offer Hope for Some

This study lends hope to the concept that intensive treatment will improve renal outcomes in at least some patients with hypertension, chronic kidney disease, and microalbuminuria.

Data from other studies also support the conclusion that intensive BP control is beneficial in select patients.

The Modification of Diet in Renal Disease trial showed that intensive BP control, compared with standard control, benefited patients who had more than 1 g of proteinuria at baseline. The ESCAPE (Effect of Strict Blood Pressure Control and ACE Inhibition on the Progression of Chronic Renal Failure in Pediatric Patients) trial also demonstrated that intensive BP control with a fixed dose of an ACE inhibitor significantly slowed the progression of renal disease, with the largest effects seen in children who had substantial proteinuria, hypertension, and a reduced GFR at baseline.

In addition, intensive BP control was beneficial in a recent study of adults in Italy who had idiopathic glomerular diseases associated with hypertension and proteinuria.

JULIE R. INGELFINGER, M.D., *is chief of pediatric nephrology at Massachusetts General Hospital, Boston, and a deputy editor of the New England Journal of Medicine. These comments were summarized from her editorial accompanying the report (N. Engl. J. Med. 2010;363: 974-6). She reported having no relevant conflicts of interest.*