Prevention and Health Services Delivery

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The most recent data from the American Heart Association estimate that >700,000 Americans have a stroke each year.1 Stroke also continues to be a major health problem in Europe and in other areas of the world. The development of more effective stroke prevention strategies continues to be an important goal.

The US public’s awareness of stroke risk and warning signs remains poor. One factor that is generally thought to provoke behavioral change is the occurrence of a stroke or myocardial infarction in a close family member. The Coronary Artery Risk Development in Young Adults (CARDIA) study measured changes in cardiovascular and stroke risk factors among 3950 young adults (aged 18 to 30 years) who either did or did not have an immediate family member with a new stroke or myocardial infarction.2 There was no effect of these events on the rates of smoking cessation, weight reduction, physical activity levels, lipid profiles, or blood pressure. Family history alone is apparently not sufficient to motivate changes in these health-related behaviors.

Black Americans are at higher risk of stroke-related mortality as compared with other Americans. The African-American Antiplatelet Stroke Prevention Study (AAASPS) investigators evaluated the baseline levels of control of cardiovascular and stroke risk factors among participants in this clinical trial.3 Of participants known to be diabetic, 33% had serum glucose ≥200 mg/dL, 48% of those without a history of hypertension had elevated blood pressures, and 24% without known hyperlipidemia had a cholesterol level ≥240 mg/dL. Considerable improvements can be made in the use of proven stroke preventive therapies in this epidemiologically high-risk population.

Several important stroke prevention trials have been published over the last year. A multifactorial intensive intervention study in patients with type 2 diabetes targeted hyperglycemia, hypertension, dyslipidemia, and micro-albuminuria with interventions including behavioral risk factor modification, and the use of a statin, angiotensin-converting enzyme inhibitor (ACEI), angiotensin-receptor blocker (ARB), and antiplatelet drug as appropriate.4 After 7.8 years, the risk of cardiovascular events was reduced by 50% with intensive treatment. There were 3 nonfatal strokes and 3 cardiovascular deaths in the 80 patients in the intensive arm versus 11 nonfatal strokes and 1 cardiovascular death in the 80 patients in the control arm (a 54% risk reduction). This result is in accord with findings from the Heart Protection Study that reported a 22% reduction in major cardiovascular events and a 25% reduction in strokes in 5963 diabetic patients treated with a statin (simvastatin) in addition to best medical care.5

Intensive blood pressure control has major beneficial effects in diabetic patients,6,7 in addition to other persons at risk of stroke.6 The Second Australian National Blood Pressure (ANBP-2) study compared an ACEI to diuretics in 6083 hypertensive patients.8 After 4.1 years, both groups achieved the same level of blood pressure control with no difference over the course of the trial. Those treated with an ACEI had fewer cardiovascular events or deaths (hazard ratio [HR] = 0.89; 95% CI: 0.79, 1.00, P = 0.05). However, a similar number of strokes occurred in each group (HR = 1.02; 95% CI: 0.78, 1.33, P = 0.91) with fatal strokes occurring more frequently in the ACEI group (HR = 1.91; 95% CI: 1.04, 3.50, P = 0.04). In the ALLHAT trial, performed in 33,357 patients, there was no difference in the primary end point between those treated with a diuretic, a calcium channel blocker (CCB), or an ACEI.9 An analysis of 7 sets of prospectively designed overviews with data from 29 randomized trials including 162,341 subjects found that, compared with placebo, strokes were reduced with treatment with an ACEI (relative risk reduction [RRR] = 28%; 95% CI: 19, 36), a CCB (RRR = 38%; 95% CI: 18, 53), or an ARB (RRR = 21%; 95% CI: 10, 31). Differences between regimens were of borderline statistical significance. There were trends toward lesser risk reductions with ACEIs versus diuretics or beta-blockers (RRR = 1.09; 95% CI: 1.00, 1.18), greater reductions with CCBs versus diuretics or beta-blockers (RRR = 0.93; 95% CI: 0.86, 1.00), and lesser reductions with ACEIs versus CCBs (RRR = 1.12; 95% CI: 1.01, 1.25), but no differences in major cardiovascular events or deaths.6 Therefore, although there may be some differences among regimens, there remain few data showing that the risk of stroke is greatly reduced with a particular class of antihypertensive. Regardless of the regimen, greater reductions in blood pressure are associated with greater reductions in stroke risk.10 Both European and North American guidelines target a blood pressure of <130/80 mm Hg in diabetic patients.11,12 The target blood pressure for secondary prevention of stroke remains <140/90 mm Hg, although one trial showed that reductions by at least 10/5 mm Hg is beneficial regardless of whether or not the patient is hypertensive.13

The optimal time to begin an antihypertensive following a stroke remains uncertain. In the ACCESS trial, candesartan started within 48 hours after stroke and continued for one year.
was compared with placebo during the first 8 days followed by candesartan.\textsuperscript{14} Although there was no difference in blood pressure control between the groups and no difference in mortality and stroke-related disability at 3 months, there was a significant benefit after 1 year in those treated early. The study needs to be replicated and further work needs to be done to help understand the results.

Consistent with the findings of 4 major trials with pravastatin and simvastatin in patients with established coronary artery disease, the GREACE trial found a 53\% reduction (RRR=0.53; 95\% CI: 0.29, 0.74, \( P=0.0017 \)) in stroke with atorvastatin (dosage adjusted to a LDL cholesterol of <100 mg/dL) compared with usual care.\textsuperscript{15} The ASCOT trial was performed in 10 305 hypertensive patients with at least 3 additional cardiovascular risk factors and total cholesterol levels <6.5 mmol/dL who were randomly assigned to receive a statin or a placebo in addition to 1 of 2 antihypertensive regimens.\textsuperscript{16} There was a 27\% reduction in fatal and nonfatal strokes in those treated with the statin after 3 years (HR=0.73; 95\% CI: 0.56, 0.96, \( P=0.024 \)). Because this benefit occurred in hypertensive subjects with normal cholesterol levels, the study strongly argues for a global cardiovascular risk approach for primary prevention of stroke. The SPARCL trial, which is in progress, specifically addresses the effects of a statin in patients with a cerebrovascular event, but no known coronary heart disease.\textsuperscript{17}

Few data are available concerning the effects of specific stroke preventive interventions in blacks. The AANSPS was designed to compare the efficacy and safety of aspirin and ticlopidine to prevent recurrent stroke among 1809 black patients.\textsuperscript{18} The study was halted when a futility analysis found a <1\% chance that ticlopidine would be superior to aspirin in the prevention of recurrent stroke, myocardial infarction, or vascular death (14.7\% of ticlopidine-treated versus 12.3\% of aspirin-treated patients had an event over 2 years, HR=1.22; 95\% CI: 0.94, 1.57). Because of a lack of difference in the primary study end point combined with an unfavorable side-effect profile, aspirin was concluded to be the better treatment in aspirin-tolerant black patients. The study underscores the importance of including adequate numbers of minority populations in stroke prevention studies.

Antioxidant vitamins are widely used by the general public. A meta-analysis of 7 randomized trials of vitamin E including 81 788 patients and 8 studies of beta carotene including 138 113 patients found neither had significant cardiovascular benefits.\textsuperscript{19} There was no reduction in stroke rates with either vitamin (3.6\% with versus 3.5\% without vitamin E, \( P=0.31 \) and 2.3\% with versus 2.3\% without beta carotene). There remains no evidence that either vitamin E or beta carotene reduces the risk of stroke.

Many studies have shown that the public’s knowledge of stroke symptoms is poor, a situation believed to contribute to the observed delays between stroke onset and a patient’s contact with the medical care system. Mass media campaigns have been viewed as one way of educating large portions of the population about stroke. A study carried out in 4 communities in Canada compared the impact of 3 different media strategies on stroke-related public knowledge.\textsuperscript{20} As in prior studies, less than half (39\% to 44\%) of those surveyed were able to name at least 2 stroke warning signs at a baseline assessment with knowledge being poorest among those >65 years of age. There was no significant change in public knowledge following a print media campaign and significant improvements after both low- and high-intensity television campaigns. However, the overall impact of the television media programs was modest, and even the television-based advertisements resulted in no significant change in knowledge among those >65 years of age. Although it is also not known whether the modest improvements in knowledge will translate into changes in patient and bystander behavior, additional studies of this type will help provide the data necessary to develop effective targeted media campaigns.

A public education campaign was incorporated into a study of the impact of a multilevel, community-based program that also included prehospital and emergency department interventions.\textsuperscript{21} The use of intravenous tissue plasminogen activator increased from 1.38\% at baseline to 5.75\% in the intervention community (\( P=0.01 \)) as compared with an increase from 0.49\% to 0.55\% (\( P=1.00 \)) in the control community. Whether the benefits of this type of aggressive program can be sustained, whether it can be successfully applied in other settings, and whether similar types of programs might be targeted to improve stroke prevention will undoubtedly be subjects for future research. Merely developing effective new stroke prevention and acute interventions will have a limited impact on stroke associated morbidity and mortality if they are not optimally incorporated into practice.

References


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