Ten Risk Factors Key to Global Stroke Risk

BY SHARON WORCESTER

FROM THE LANCET

Ten distinct risk factors account for about 90% of global stroke risk, according to findings from the first phase of INTERSTROKE, a multinational, case-control study that has enrolled 6,000 patients and controls thus far.

The findings, which suggest that the stroke burden could be substantially reduced by targeted interventions to address the identified risk factors, were published online in the Lancet, and were reported simultaneously at the World Congress of Cardiology in Beijing.

Five of the risk factors that were found to be significantly associated with stroke risk accounted for about 80% of the population-attributable risk for all stroke; these were self-reported hypertension, current smoking, abdominal obesity (highest vs. lowest tertile of waist:hip ratio), diet (highest vs. lowest diet risk score), and regular physical activity. These comparisons yielded odds ratios of 2.64, 2.09, 1.65, 1.35, and 0.69, respectively.

The addition of another five significant risk factors that were identified in this study further increased the population-attributable risk for all stroke associated with these risk factors to 90%. These additional risk factors (diabetes, alcohol intake of more than 30 drinks per month/binge drinking, psychosocial stress/depression, cardiac causes, and highest vs. lowest tertile of the ratio of apolipoproteins B to A1) generally increased the odds of stroke by a smaller amount than did the other five risk factors that accounted for a greater proportion of the population-attributable risk. The comparisons yielded odds ratios of 1.36, 1.51, 1.30/1.35, 2.38, and 1.89, respectively.

All risk factors identified in this study were significantly associated with ischemic stroke, whereas hypertension, smoking, waist:hip ratio, diet, and alcohol intake also were significantly associated with intracerebral hemorrhagic stroke, Dr. Martin J. O'Donnell of McMaster University, Hamilton, Ont., and his colleagues reported (Lancet 2010 June 18 [doi:10.1016/S0140-6736(10)60834-3]).

In an effort to establish the association of conventional and emerging risk factors with stroke, the INTERSTROKE researchers set out to perform a study similar to the INTERHEART study published in 2004, which identified nine modifiable risk factors that explained the majority of myocardial infarctions worldwide.

Between March 1, 2007, and April 23, 2010, the investigators studied 3,000 patients from 22 countries, and 3,000 sex- and age-matched controls with no stroke history. Case patients (2,337 with ischemic stroke and 663 with intracerebral hemorrhagic stroke) presented with acute first stroke, and were enrolled within 5 days of symptom onset and 72 hours of hospital admission. A structured questionnaire and physical examination, including routine neuroimaging, were performed in all patients.

"Our study provides essential information on the importance of common, potentially modifiable vascular risk factors, and builds on previous epidemiological studies," they wrote, noting that although the risk factors are similar to those identified as being associated with MI in INTERHEART, hypertension, apolipoproteins, physical activity, and alcohol intake appear to have different relative importance for stroke vs. myocardial infarction.

"These findings are important to help guide optimum selection of risk-factor targets for population-based programs to prevent all cardiovascular diseases," they concluded. ■

VITALS

Major Finding: Ten factors that were found to be associated with stroke risk were self-reported hypertension, current smoking, abdominal obesity, diet, regular physical activity, diabetes, alcohol intake of more than 30 drinks per month/binge drinking, psychosocial stress/depression, cardiac causes, and highest vs. lowest tertile of the ratio of apolipoproteins B to A1.

Data Source: Phase I of INTERSTROKE, a large, multinational, case-control study of 3,000 patients and 3,000 controls.

Disclosures: This study was funded with unrestricted grants from the Canadian Institutes of Health Research, Heart and Stroke Foundation of Canada, Canadian Stroke Networks, Pfizer Cardiovascular Award, Merck & Co., AstraZeneca, and Boehringer Ingelheim. Multiple authors reported receiving grant/research support, honoraria, expenses, and/or fees from numerous pharmaceutical companies (including those also listed as funding sources for this study), and from other sources, and/or being associated with the American Heart Association as a board member and officer.

VIEW ON THE NEWS

Data May Spur Prevention Strategies

Stroke is the second-leading cause of death globally, and the cause of more than 85% of deaths in developing countries. Therefore, research on risk factors for stroke around the world is imperative for addressing the problem.

The INTERSTROKE investigators confirmed that hypertension is the leading risk factor for stroke not only in high-income countries, but also in developing countries.

This finding is especially relevant because it highlights the need for regional health authorities to develop strategies to screen the general population for high blood pressure and offer affordable treatment to reduce the burden of stroke.

The INTERSTROKE study – although limited by its matched case-control design vs. a prospective cohort approach – nonetheless represents an efficient approach to obtaining useful information about stroke risk. The important findings of this study should help inform worldwide stroke prevention strategies and reduce the global burden of stroke.

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Teriflunomide Lowers Annualized Relapse Rate 30% in MS

BY SHARON WORCESTER

FROM THE ANNUAL CONGRESS OF THE EUROPEAN COMMITTEE FOR TREATMENT AND RESEARCH IN MULTIPLE SCLEROSIS

Teriflunomide, a novel oral disease-modifying drug, significantly reduced the annualized relapse rate and the risk of disability progression in relapsing multiple sclerosis by about 30% in a 2-year, phase III trial.

The study of Teriflunomide in Reducing the Frequency of Relapses and Accumulation of Disability in Patients With Multiple Sclerosis (TEMSO), which was sponsored by Sanofi-Aventis, randomized 1,088 patients to receive a single daily dose of 7 mg or 14 mg of teriflunomide or placebo.

The primary end point – the annualized relapse rate – was significantly lower among the 7-mg and 14-mg groups (0.370 and 0.369, respectively) than it was in placebo-treated patients (0.539). These rates represented a statistically significant reduction of 31% compared with placebo. Patients in the 14-mg group also experienced a significant 30% reduction in the risk of disability progression, Dr. Paul O'Connor reported at the congress.

Teriflunomide is the active metabolite of leflunomide, a synthetic, low-molecular-weight drug that was approved by the Food and Drug Administration in 1998 for the treatment of rheumatoid arthritis.

The metabolite is a reversible inhibitor of the mitochondrial enzyme dihydro-orotate dehydrogenase (DHODH) that exerts anti-inflammatory, antiproliferative, and immunosuppressive effects, but the mechanisms by which it does so are not yet completely understood. Inhibition of pyrimidine biosynthesis (via suppression of DHODH) and interference with tyrosine kinase activity both appear to be involved.

The treatment groups also experienced a significant reduction in brain disease activity as measured by magnetic resonance imaging (MRI). The burden of disease as determined by total lesion volume, for example, was reduced by 39% and 67% in the 7-mg and 14-mg dose groups, respectively, compared with placebo, said Dr. O'Connor of St. Michael's Hospital, Toronto. He is the principal investigator for TEMSO.

"In my view, teriflunomide is a safe and effective new monotherapy, and it represents a potential first-line treatment for patients with relapsing MS," he said during a press briefing on the findings.

The safety profile of teriflunomide in this study was a particularly strong, positive point, he added.

The overall adverse event rates were the same in the placebo and treatment groups, as were the rates of adverse events leading to permanent discontinuation of treatment. Patients in the teriflunomide group experienced more nausea, diarrhea, increases in alanine transferase, and hair thinning than did those in the placebo group, but these effects were mild. Treatment was generally very well tolerated, and no opportunistic infections occurred.

Dr. Mark Freedman of the Multiple Sclerosis Research Clinic at Ottawa (Canada) Hospital said the results from a second phase III study of teriflunomide are expected to be reported in 2012. He and Dr. Comi are investigators in the TEMSO trial. ■

VITALS

Major Finding: Compared with the placebo group, those in both the 7-mg and 14-mg teriflunomide groups experienced a statistically significant 30% reduction in the annualized relapse rate, which was the primary end point.

Data Source: A randomized, placebo-controlled phase III study (TEMSO) involving 1,088 patients with relapsing MS.

Disclosures: Sanofi-Aventis sponsored the trial. Dr. O'Connor, Dr. Comi, and Dr. Freedman disclosed financial relationships with many companies that manufacture drugs for MS, including Sanofi-Aventis.