with different antiplatelet mechanisms are more effective than either antiaggregant alone. However, both questions deserve further scrutiny.

H. Tohgi, MD
S. Konno, MD
K. Tamura, MD
B. Kimura, MD
Department of Neurology
Iwate Medical University
Morioka, Japan

K. Kawano, PhD
Department of Endocrinology
Scientific Research Laboratory
Tokyo, Japan

References

Response
While we appreciate the comments of Drs Samuelsson and Svensson, we will further elucidate our view of the role of aspirin treatment in the prevention of stroke.

1. Given the varied etiologies of the three mechanisms of ischemic stroke (thrombosis, embolism, and decreased perfusion) no one would expect aspirin to address the prevention of all strokes. For those circumstances in which white clot (platelet-fibrin rich) formation is to be prevented, an antiplatelet agent would be expected to be effective. As platelet aggregation and activation may be highly shear dependent, circumstances in which high shear rates exist would not be expected to respond to aspirin because platelet aggregation depends mostly on a non-cyclooxygenase-dependent pathway. Ticlopidine may be the more appropriate agent under these circumstances. Where cyclooxygenase-dependent platelet aggregation may occur is the proper circumstance under which aspirin may contribute to the prevention of white clot. Our study suggests that the optimal dose of aspirin to prevent cyclooxygenase-dependent platelet aggregation depends on the individual receiving the aspirin. While low-dose aspirin (75 mg/d) may provide a risk reduction of stroke at the lowest common denominator for all, it may not achieve the maximum effect in each individual.

2. While our study used platelet aggregation inhibition as assessed by aggregometry using ADP, EPI, collagen, and AA, we recognize that this test may not measure shear-induced or otherwise induced platelet aggregation. We are unaware of any study that has shown bleeding time or any other measure of aspirin efficacy to be the clinically significant test. In fact, it may be that given the desired object of antiplatelet effect (for example, inhibition of shear-induced aggregation), each circumstance may define the appropriate test to be applied to assess the efficacy of a given drug to achieve that effect. The bleeding time test may not be sensitive enough to detect dose response in this regard.

3. Those patients in our study who failed aspirin treatment, as defined in our study, did so because complete inhibition of platelet aggregation was not enough or appropriate for their stroke mechanism and etiology. Although our study did not prospectively attempt to elucidate the stroke mechanism in these patients, aspirin failure should alert the clinician to the need to search for other mechanisms of stroke in the patient (eg, high shear, tight stenosis, stasis-red clot) which may be responsive to alternative therapies.

4. Finally, while some patients may need higher doses of aspirin as their dose is individualized, surely the risk of hemorrhage may be outweighed by the beneficial effect of preventing a stroke which at least at present is a condition more difficult to treat. To assess whether aspirin is working, like coumadin, it may be preferable to think in terms of antithrombotic effect and not dosage.

Cathy M. Helgason, MD
Associate Professor of Neurology
Director of Cerebrovascular Service
University of Illinois at Chicago
College of Medicine
Hospital and Clinics

Kathryn Tortorice, PharmD
Clinical Assistant Professor
University of Illinois at Chicago
College of Medicine and Pharmacy
Hospital and Clinics
Chicago, Ill

Increased 99mTc-HMPAO Uptake in Ischemic Stroke

99mTc-labeled d, l-hexamethylpropylene amine oxime (HMPAO) hyperfixation relative to 113Xe-measured blood flow in three patients during the subacute phase of stroke was recently described by Sperling and Lassen,7 who indicated that the interpretation of scans during this phase may be misleading. This finding highlights the importance of elucidating the uptake and retention mechanism of 99mTc-HMPAO in repurposed as well as normal and ischemic brain.2 We are most interested to know whether the authors have performed combined 99mTc-HMPAO and 113Xe studies during the acute phase (<48 hours) of ischemic stroke.

Our experience has been that increased 99mTc-HMPAO uptake (defined as a perfusion level >12% of the homologous region of interest in the unaffected cerebral hemisphere when measured by side-to-side ratios) is much less common during this phase. In a series of 170 consecutive patients studied within 48 hours of stroke onset (all subtypes), increased 99mTc-HMPAO uptake was seen in 6.5% (11 patients). In nine patients the area of increased uptake was restricted to a focal area of cerebral cortex. In two increased uptake extended over the middle cerebral artery cortex in the setting of rapid neurological improvement from a syndrome of profound hemispheric ischemia (so-called “spectacular shrinking deficit”).3 Regions of increased uptake usually had normal computed tomographic (CT) topography at 7 to 14 days. In contrast, during the subacute phase (7 to 28 days) areas of increased 99mTc-HMPAO uptake were present in 48% of the patients (12 of 25) and in most cases occurred at the site of infarction on CT. We have never encountered increased 99mTc-HMPAO uptake after 28 days.

Increased 99mTc-HMPAO uptake is much less common during the acute phase of stroke and is often associated with tissue preservation. It is quite possible that the hyperfixation described during the subacute phase is uncommon during the acute phase. We await the results of the ongoing studies with much interest.

A.E. Baird, MD
G.A. Donnan, MD
Austin Hospital
Heidelberg, Victoria, Australia
Increased 99mTc-HMPAO uptake in ischemic stroke.
A E Baird and G A Donnan

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