Arterial Ischemic Stroke in Children
Baby Steps

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Arterial ischemic stroke (AIS) in a child can have devastating, lifelong sequelae.1 Given the infrequency of AIS (approximately 3 per 100,000 children2), primary prevention is probably not feasible in the absence of a known risk factor. However, the prevention of recurrent AIS in childhood, ie, secondary prevention, may be feasible. How can recurrent childhood AIS be prevented? Current consensus guidelines on the use of antiplatelet and anticoagulant therapy for AIS in children are not based on randomized controlled trials (RCTs).2,3 Detailed knowledge of the rates and predictors of AIS recurrence in children is essential before appropriate RCTs can be designed and before rational treatment guidelines can be promulgated. The article by Ganesan et al4 in this issue of Circulation provides new information in this regard.

The greatest strength of the study by Ganesan et al4 is that clinically apparent and clinically silent recurrences are both clinically apparent and clinically silent recurrences are common after first AIS in childhood. Some5,6 but not all7 previous large studies of childhood AIS have reported a lower incidence of clinical recurrence. For example, a previous large (301 patient) prospective study of childhood AIS by Sträter et al5 reported a lower clinical recurrence rate of 6.6%, but this study included a smaller proportion of children with preexisting diagnoses; also, unlike the study by Ganesan et al,4 it excluded children with previous vascular events (including TIAs) and, importantly, sickle cell disease (which is associated with a very high rate of recurrent AIS).

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The greatest strength of the study by Ganesan et al4 is that 179 (84%) of the 212 children with AIS, including 103 who remained asymptomatic, underwent repeat neuroimaging (magnetic resonance imaging or CT) at least a year after AIS. Patients underwent repeat neuroimaging (magnetic resonance imaging or computerized tomography [CT]) at the time of clinical recurrence or, if asymptomatic, at least a year after AIS. Cox and logistic regression analyses were used to explore the relationships between risk factors and clinical and radiological recurrence. Of the 212 patients with AIS, 97 were in the prior diagnosis group. Seventy-nine of the 212 (37%) had a clinical recurrence (29, stroke; 46, transient ischemic attack [TIA]; 4, death with reinfarction) between 1 day and 11.5 years (median 267 days) later. After 5 years, only 59% of patients were free of recurrence. Moyamoya disease shown by angiography and low birth weight were independently associated with clinical recurrence in the whole group. Genetic thrombophilia was associated with clinical recurrence in previously healthy patients independently of the presence of moyamoya disease. Sixty of 179 patients who underwent repeat neuroimaging had radiological reinfarction, which was clinically silent in 20 patients. Previous TIA, bilateral infarction, prior diagnosis (specifically immunodeficiency), and leukocytosis were independently associated with radiological reinfarction. Previous TIA and leukocytosis were also independently associated with clinically silent reinfarction.

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Evidence-Based Guidelines for the Treatment of AIS in Children

Children with AIS are often treated with antiplatelet agents (aspirin or clopidogrel) or anticoagulants (heparin or warfarin). Attempts at evidence-based guidelines for the treatment of AIS in children remain empiric, however, because of the lack of RCT data. The effects of treatment on AIS recurrence rates cannot be determined from the study by Ganesan et al because patients were not randomized to treatment versus no treatment. The only treatment for childhood AIS that is supported by a RCT is long-term transfusion therapy in sickle cell disease. Pediatric treatment guidelines for AIS are largely extrapolated from recommendations for adults, in whom AIS is much more common and in whom numerous large RCTs have therefore been performed. However, the most common underlying pathophysiology of adult AIS (atherosclerosis) is profoundly different from those in childhood AIS (congenital heart disease, sickle cell disease, prothrombotic abnormalities in the hemostatic system, mechanical injury with arterial dissection, local inflammatory arteriopathy, and moyamoya disease).

Only RCTs building on the data of pediatric outcome studies such as that by Ganesan et al will result in truly evidence-based guidelines for the treatment of childhood AIS. Although rare, the incidence of AIS in children is similar to that of brain tumors, and coordinated multicenter RCTs of pediatric brain tumors have been successfully undertaken. The formation of national and international networks focused on pediatric stroke research are steps in the right direction.

Disclosures

None.

References


Key Words: Editorials • ischemia • stroke • pediatrics • prevention
Arterial Ischemic Stroke in Children: Baby Steps
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Circulation. 2006;114:2094-2095
doi: 10.1161/CIRCULATIONAHA.106.659219
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2006 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/114/20/2094

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