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Topical Review

Guidelines for Urgent Management of Stroke in Children

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ABSTRACT

Stroke in children carries lasting morbidity. Once recognized, it is important to evaluate and treat children with acute stroke efficiently and accurately. All children should receive neuroprotective measures. It is reasonable to consider treatment with advanced thrombolytic and endovascular agents. Delivery of such care requires purposeful institutional planning and organization in pediatric acute care centers. Primary stroke centers established for adults provide an example of the multidisciplinary approach that can be applied to the evaluation and treatment of children who present with acute stroke. The organizational infrastructure of these centers can be employed and adapted for treatment of children with acute stroke. It is likely that care for children with acute stroke can best be delivered by regional pediatric primary stroke centers dedicated to the care of children with pediatric stroke.

Keywords: stroke, pediatric, emergency department, stroke center

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Although both children and adults can experience strokes that affect very similar vascular territories in brain and share similar features on neuroimaging, the course of clinical management of the patient in each age group can vary considerably. An adult who suddenly develops typical symptoms of a stroke such as hemiparesis, aphasia, ataxia, or hemianopsia comes to medical attention quickly, often is assessed in the field and in hospital by teams with special training in the evaluation and care of adults with stroke, and is treated in a medical center designated as a primary stroke center. Children with stroke, in contradistinction to adults, encounter delay in their delivery to medical attention. Once in a medical setting, the acute neurological deficit often is not recognized, and stroke as etiology of presenting signs and symptoms is often not considered. Consequently, children who have stroke encounter considerable delay before acquisition of diagnostic imaging. Examination of the diagnostic process for children in the emergency department and on the inpatient service who have had stroke revealed considerable diagnostic delay due to failure to include stroke in the differential diagnosis.[1-3]

We will examine the development of adult primary acute stroke centers. Next, features that compel the development of multidisciplinary acute stroke programs for children will be presented. Subsequently, a method for construction of a

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pediatric stroke center and components of care for children with acute arterial stroke will be considered. Finally, these features will be illustrated through presentation of an actual patient with acute arterial stroke who was treated successfully with tissue plasminogen activator (tPA).

The first decade of the twenty-first century brought transformation in acute stroke care for adults, and more than half of all adults access to care at a primary stroke center.[4] Indeed, an adult with acute stroke may be evaluated and treated in the field by an emergency medical team especially trained in the care of patients with acute stroke. Communication between the field team and the hospital-based primary stroke center medical team will facilitate the arrangement of emergency room, neuroradiological, pharmacologic, or interventional services even before the patient arrives to the hospital (analogous to primary coronary intervention in acute myocardial infarction).

Children with acute stroke should be diagnosed within 4.5 hours following symptom onset so that thrombolytic treatment[5,6] or thrombectomy might be administered.[7] Administration of tPA facilitates degradation of fibrin in thrombus and can lead to early recanalization of an artery occluded by thrombus. Although the use of tPA treatment for adults with acute stroke is established, experience with its use in children remains limited. Questions remain regarding its use in patients younger than two years, at times greater than 4.5 hours from stroke onset, and in those at either extreme of clinical severity.

Studies in adults have revealed that despite an increased risk of fatal intracranial hemorrhage during the first few days after treatment, tPA significantly improves the likelihood of a favorable outcome when administered within 4.5 hours of stroke onset in appropriately selected patients. Moreover, it appears that earlier treatment correlates with better outcome.[8] Potential adverse effects of tPA include idiosyncratic nausea, vomiting, bradycardia, fever, allergic response, cardiac arrhythmia, and hypotension (in up to 10%).[9] Life-threatening nonidiosyncratic side effects consist of hemorrhage in gastrointestinal (5% of patients), genitourinary (4%), or central nervous system (6.4%). Symptomatic intracranial hemorrhage, in particular, remains a concern following administration of tPA in patients. The Alberta Stroke Program Early CT Scoring (ASPECTS) scheme has proved accurate and useful in identifying stroke size in the middle cerebral artery (MCA) territory on head computed tomography (CT) and in the estimation of the likelihood of occurrence of symptomatic intracranial hemorrhage following treatment with tPA.[5,10] Magnetic resonance imaging (MRI) and diffusion-weighted imaging (DWI) specifically are even more sensitive than CT in the detection of acute stroke.[11] However, as found with head CT, the size of DWI abnormality was found to correlate directly with the likelihood of symptomatic intracranial hemorrhage following tPA therapy.[12]

Recent developments in endovascular therapy of adults with stroke have reverberated across the field of pediatric stroke. The Multicenter Randomized CLinical trial of Endovascular treatment for Acute stroke in the Netherlands (MR CLEAN) multicenter study of endovascular therapy administered to adults with proximal large cerebral artery occlusion many of whom had already been treated with intravenous tPA demonstrated not only more rapid arterial recanalization but also superior outcome compared with standard medical therapy.[13] These results were confirmed in both Endovascular Treatment for Small Core and Anterior Circulation Proximal Occlusion with Emphasis on Minimizing CT to Recanalization Times (ESCAPE) as well as Solitaire with the Intention for Thrombectomy as Primary Endovascular Treatment (SWIFT PRIME) studies.[9,14] The exciting results from these studies have revealed endovascular therapy and thrombectomy to be first-line treatments for acute stroke in adults with large cerebral vessel occlusion. Although exciting for adults with stroke, the role of this therapeutic procedure in children with acute stroke is not yet clear.

In adults, the benefit of treatment by a medical team organized and trained in the care of patients with acute stroke extends beyond the use of intravenous tPA or endovascular therapy. Patients treated in primary stroke centers follow an improved clinical course compared with those treated by clinicians not organized into stroke teams. Lower mortality rate, readmission rate, and complication rate and shorter length of in-patient stays have been observed in patients treated at adult primary stroke centers.[15-17] These features argue strongly for a similar approach to care of children with acute stroke.

Reason to emulate the adult experience of acute stroke care in children

Stroke, although regarded by many to be rare in children, is not. Both prevention of mortality and attenuation of morbidity constitute potent reasons to optimize the ability to recognize and to treat rapidly children with stroke. Cerebrovascular disease represents one of the ten most common causes of mortality in patients ranging in age from five through 24 years.[18] Although stroke occurs with a frequency 175 to 200/100,000 among adults, stroke occurs in children older than one month as frequently as 13/100,000 per year.[19] The stroke incidence is higher in neonates (25 to 40/100,000 births) and is highest among premature infants (up to 100/100,000 births).

The morbidity in children following arterial stroke is considerable. As many as 50% of neonates and 65% of children older than 1 month sustain lasting motor deficits as a consequence of stroke. Furthermore, up to 60% of children who have had neonatal stroke demonstrate cognitive deficits, especially those of executive function and language. Similarly, half of children who have stroke at greater than age one month have been found to have cognitive deficits.[20-24]

The mortality rate for children with stroke is one third that found in adults with either ischemic or hemorrhagic stroke. Consequently, a much higher proportion of children than adults carry the consequences of their cerebral injury for decades.[25-28] The cost for care of children who have had a stroke at either in the neonatal or at an older age appears to be both high and sustained.[27] Consequently, the aggregate cost for care of a patient with stroke is likely greater for a child than for an adult.[29]

Organization for a primary pediatric stroke center: Just little adult centers?

The morbidity and mortality associated with cerebrovascular disease argues convincingly for mobilization of