Pediatric Neurology 56 (2016) 18–24

Contents lists available at ScienceDirect

Pediatric Neurology

journal homepage: www.elsevier.com/locate/pnu

Topical Review

Preparing for a "Pediatric Stroke Alert"

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ABSTRACT

BACKGROUND: Childhood arterial ischemic stroke is an important cause of morbidity and mortality in children. Hyperacute treatment strategies remain controversial and challenging, especially in the setting of increasingly proven medical and endovascular options in adults. Although national and international pediatric guidelines have given initial direction about acute therapy and management, pediatric centers have traditionally lacked the infrastructure to triage, diagnose, and treat childhood arterial ischemic stroke quickly. **METHODS:** In the past 10 years, researchers in the International Pediatric Stroke Study and Thrombolysis in Pediatric Stroke study have initiated early strategies for establishing pediatric specific stroke alerts. **RESULTS:** We review the rationale, process and components necessary for establishing a pediatric stroke alert. **CONCLUSION:** Development of pediatric stroke protocols and pathways, with evidence-based acute management strategies and supportive care where possible, facilitates the evaluation, management, and treatment of an acute pediatric stroke.

Keywords: arterial ischemic stroke, pediatric stroke centers, childhood stroke, TIPS trial

Pediatr Neurol 2016; 56: 18-24

Introduction

Childhood arterial ischemic stroke (AIS) occurs in 1 to 2 children per 100,000 per year, accounting for approximately 1000 childhood strokes in the United States per year.[1] Although national and international guidelines have given initial direction about acute therapy and management, pediatric centers have traditionally lacked the infrastructure to triage, diagnose, and treat childhood AIS quickly.[2,3] In addition, these guidelines can become outdated in the current landscape of rapidly changing adult stroke clinical trials. The challenges in preparing to accurately diagnose and manage acute childhood AIS are many, including the infrequency of childhood AIS, the lack of data to inform management despite the increasing evidence for acute therapies in adults, and the lack of community awareness of

Article History:
Received July 24, 2015; Accepted in final form October 13, 2015

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http://dx.doi.org/10.1016/j.pediatrneurol.2015.10.012

stroke occurring in childhood. Although readiness for the management of childhood stroke in the United States and Canada has increased dramatically in the past decade following the formation of the International Pediatric Stroke Study (IPSS) consortium and the subsequent Thrombolysis in Pediatric Stroke (TIPS) trial,[4,5] preparedness for acute childhood AIS is difficult and treatment decisions remain controversial. This article reviews the current rationale for an acute childhood stroke pathway (or "Stroke Alert/Code Stroke"), and shares our experience with designing a Pediatric Stroke Alert system and pediatric stroke centers.

Acute interventions for childhood stroke remain highly controversial, with the 2008 American Heart Association Guidelines recommending, "until there are additional published safety and efficacy data, tPA generally is not recommended for children with AIS outside a clinical trial (Class III, Level of Evidence C)."[4] However, there was no consensus about the use of tissue plasminogen activator (tPA) in older adolescents who otherwise meet standard adult tPA eligibility criteria."[1] Similarly, The American College of Chest Physicians (CHEST) guidelines also recommend "against the use of thrombolysis (tPA) or mechanical thrombectomy outside of specific research protocols (Grade 1C)."[2] Despite these cautionary guidelines, tPA is administered in the United States in up to 2% of all children with acute stoke.[6,7] Indeed, many of the pioneers in the childhood stroke field have published their experience with administration of intravenous (IV) tPA, as well as intra-arterial therapies.[8-10] This paradox is likely secondary to several factors, including provider comfort with recommending aggressive therapies and increasing evidence about the efficacy of hyperacute systemic and intra-arterial therapies for acute adult stroke. Indeed, the recent evidence demonstrating the effectiveness of endovascular therapies in adult stroke introduces even more uncertainty into these decisions in children.[11-14] This ambiguity highlights the need for pediatric stroke centers or units to provide the infrastructure necessary to improve access to acute stroke therapies and trials, provide safe and effective therapies, and improve stroke outcomes.

If tPA is given to children, it is clear that is should be administered in the setting of a prepared center that is familiar with adult and child hyperacute guidelines. The early IPSS literature underscores this point, because before the advent of standardized protocols at most of these centers, children with stroke were sometimes treated outside of standard tPA guidelines. In the original IPSS cohort of 687 children with arterial ischemic stroke presenting from 2003 to 2007, at least four of the 15 children who were administered IV (nine) or intra-arterial (six) tPA, received treatment outside of standard adult time treatment guidelines.[7] This series also reported that there were no deaths or symptomatic intracranial hemorrhage in these children, suggesting tPA in children may be safe. There is convincing evidence that the establishment of organized adult inpatient units has improved outcomes, including survival and reduced morbidity.[15] Advanced preparation for acute childhood AIS is important for comprehensive and standard stroke care and enhances a provider's comfort with acute stroke decision making. Hyperacute therapy should only occur in a center that has prepared for this possibility beforehand.

In order to address the lack of evidence about tPA treatment in children with stroke, the IPSS initiated the TIPS trial in 2012.[16] The TIPS trial was a phase 1 multicenter cohort study that examined the safety and dosing of IV tPA in children aged 2 through 17 years.[17] Although the trial closed secondary to poor enrollment, the centers participating in the trial reported several important findings from this trial. Centers that participated in the TIPS trial reported a significant increase in self-reported stroke readiness from 6.2 to 8.7 on a 10-point Likert scale (with 10 being completely ready), recording that this change in stroke readiness was secondary to the creation of stroke triage protocols, stroke alerts, and stroke order sets.[4] Importantly, no child was given tPA outside of standard adult treatment time points, as had been previously reported by the IPSS series from 2003 to 2007.[7] In addition, each center created 24/7 rapid-response teams possessing neurovascular expertise, a centerpiece to their capabilities to consider hyperacute therapies and initiate standard stroke management. Indeed, early treatment decisions surrounding fluid management, treatment of hyperthermia, antithrombotic management, and prevention of hyperglycemia may be more essential in improving childhood AIS outcomes than preparing for tPA administration,[18] as the majority of children with AIS do not present in time for acute interventions.[16,19] As such, an essential piece of "readiness" is to rapidly bring the expertise of the stroke-oriented child neurologist (or an adult vascular neurologist) in order to expedite diagnosis and treatment decisions. In addition, when considering stroke as a diagnosis in a child, it is important to provide the right treatment to the right person at the right time. Stroke mimics in pediatric stroke are common and are more often malignant than benign, and can include seizure, metabolic stroke, postictal paralysis, acute disseminated encephalomyelitis, tumor, cerebellitis, drug toxicity, idiopathic intracranial hypertension, subdural empyema, arteriovenous malformation (AVM), or intracranial abscess.[20] The operation of an acute stroke pathway therefore offers the prospect for improving timeliness and specificity of a diagnosis and treatment for a wide variety of childhood neurological emergencies.

It has also been our experience that increased readiness for childhood stroke brings enhanced visibility to the family of the neurologist's participation, and that this can improve the coping response of families to their child's illness as well. A lack of readiness can lead to diagnostic and therapeutic uncertainty and/or a lack of initial counseling for families leading to increased familial distress. When families are not counseled accurately about hyperacute therapies in the acute setting, they are sometimes concerned by perceived inaction, even though childhood stroke recommendations do not endorse IV tPA and endovascular therapies, and these therapies are rare in children.[1,2] The fact that litigation surrounding adult stroke is much more likely from a lack of action (i.e., not giving tPA) than an adverse reaction to therapy is telling.[21] Although not giving tPA to a child is always a defensible position given current recommendations, explaining this rationale to the family at the time of diagnosis is crucial to building trust with the family.