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Seizures are Common in the Acute Setting of Childhood Stroke - A Population-Based Study

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Abstract

In our large population-based cohort, 3.1% of adults had seizures within the first 24 hours of acute stroke. The objective of our study was to determine a similar incidence in children and compare by stroke subtype. Stroke cases in children between 7/93-6/94, and 1/99-12/99 were retrospectively identified and abstracted. We identified 31 strokes during the two study periods, including 17 ischemic strokes, 12 intracerebral hemorrhages, and 2 subarachnoid hemorrhages. Seizures occurred within 24 hours of the stroke in 58% (18/31) of children. No significant differences where found in the rate of seizure by stroke subtype. The relative risk (95% CI) for seizure in the acute stroke setting in children vs. adults is 18 (95% CI: 13, 26). As compared to adults, seizures within the acute setting of childhood stroke are common with an occurrence rate in our population of 58%.

Keywords

seizures; cerebrovascular disease; stroke; childhood

The relationship between seizures and stroke was reported as early as 1864 by John Hughlings Jackson.[1]. Subsequent reports estimated an incidence of seizures after stroke of 0.4 to 43% in the adult population. [2-13]. In children, the reported incidence of seizures in the setting of acute stroke varies from 34 -53.8%. However, these studies were not population-based, and the defined time-frames for incidence of seizure were quite variable.[17-24]. In addition, there was great variability regarding patient attributes, diagnostic criteria, and duration of follow-up. In the Greater Cincinnati/ Northern Kentucky population, which is the basis of the current study, 3.1% of adults had seizures in the setting of acute stroke; seizures occurred more frequently in patients with hemorrhagic stroke. [15]. Research has identified stroke as a clear risk factor for seizure development in the elderly[14], but in children this relationship has not been clearly established.[17-24].

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In this population-based childhood study we sought to determine the incidence of seizures within the first 24 hours of stroke, including ischemic strokes and intracranial hemorrhage. The population studied is representative of the United States with regard to median age, percent black and socioeconomic indicators. [25]. Based on the higher incidence of epilepsy in children in general, we hypothesized that the incidence of seizures in this setting would be higher in children than in adults. Based on our adult data, we also hypothesized that there would be no racial differences in the incidence of seizures. Further, because of the population-based study design, our data should provide the best estimate the occurrence of acute seizures within the first 24 hours of noted stroke symptoms in the U.S. population.

Methods

Detailed methods of the Greater Cincinnati/Northern Kentucky Stroke Study (GCNKSS) have been previously published. [25-26]. The study population is defined as all residents of the Greater Cincinnati/Northern Kentucky region, which includes two southern Ohio counties and three contiguous Northern Kentucky counties that abut the Ohio River. This study was approved by the Institutional Review Board at all participating hospitals.

The GCNKSS involved ascertainment of all stroke events that occurred in the population between 7/1/93 and 6/30/94, and again in calendar year 1999. Study nurses screened the medical records of all inpatients with primary or secondary stroke-related ICD-9 discharge diagnoses of 430-436 from the acute-care hospitals in the study region. We additionally screened ICD-9 codes 437 and 438 at only Cincinnati Children's Hospital to try to ensure that strokes were not missed. There is however significant limitations to identifying stroke in children using ICD-9 codes as described by Golomb et al. [27].

To qualify as a GCNKSS case, a patient must have been younger than age 18 years old, and must have met the criteria for one of the five stroke categories adapted from the Classification for Cerebrovascular Diseases III28. and from epidemiological studies of stroke in Rochester, MN[29] : cerebral ischemia, intracerebral hemorrhage, subarachnoid hemorrhage, stroke of uncertain cause, or transient ischemic attack. Strokes of prematurity (e.g. germinal matrix hemorrhages) excluded. Once potential cases were identified, the study nurse abstracted information regarding demographics (including self-reported race), stroke symptoms, all relevant times (including time of symptom onset, last time that patient noted to be normal and arrival in the ED), and other relevant clinical information. A study physician reviewed every abstracted case and all available neuro-imaging studies to verify the occurrence of a stroke or TIA, and assign a stroke subtype. Stroke onset was determined at the time the child was noted to have any focal neurological deficit, often in children this would be parental report with a note when child was last seen as “normal” as in the case of focal deficits upon awakening from sleep. All seizures occurring within 24 hours of presentation of stroke symptoms were defined as “acute.” All seizure types were included.

The abstracted strokes were compared by stroke subtype and by age at presentation.

Statistical Analysis

Exact tests were used to compare adult and childhood acute stroke rates due to the small numbers, the datasets from 1993-94 and 1999 were combined, so inclusion period was considered as a covariate. To analyze the significance of observed differences between the patients who developed seizures and those that did not, a bivariate analysis was performed on the demographic characteristics using chi-square or Fisher's exact test for categorical variables and the student's t-test or Wilcoxon rank sum test for continuous variables, dependent upon the distribution.

Results

We found a total of 31 strokes during the two study periods. There were 17(55%) ischemic strokes (IS), 12 (39%) intracerebral hemorrhages (ICH), and 2 (6%) subarachnoid hemorrhages (SAH). Of these patients, 18/31 (58%) had seizures during the acute setting of stroke. There were no significant differences in the rate of seizures by stroke subtype (p=0.53), gender or age (Table 1).

The youngest children trended towards having higher rates of early seizure in the stroke setting: of the 13 strokes between 0 and 5 years, 9(69%) had early seizures, compared to 9/18 (50%) in those 6 years and older (p=0.28).

We previously reported a seizure rate within 24 hours of acute stroke of 3.1% for adults. Here we show that children had a seizure rate of 58% in the acute stroke setting. Compared to adults, the relative risk (95% CI) for acute seizure in children was 18 (95%CI 13, 26; p=0.0001).[15].

Discussion

Our study provides the first population-based comparison of adult and childhood seizure rates in the setting of acute stroke. We found that seizures were 18 times more likely in children than adults within 24 hours of noted stroke symptoms and we showed that there is no difference in acute seizure rates by stroke subtype, unlike the adult population where seizures were more common with hemorrhagic strokes. We also found a non significant trend that the rate of seizure varied by patient age, with the youngest patients having the highest incidence of seizure. Work done by Zimmer et al, demonstrates the age trend with seizures being more frequent in younger children when looking at childhood arterial ischemic stroke.[16].

Wide ranges exist in the literature regarding the incidence of early seizures in children following stroke, ranging from 34 to 53.8%. [17-24]. These differences are likely related to case ascertainment and the inclusion and exclusion criteria. By including neonatal stroke and all stroke subtypes, our estimate of 58% is likely to be more inclusive than prior studies, and reports the first population-based incidence of seizures after acute stroke in the pediatric population.

The occurrence of higher seizure rates in children than in adults is likely due to immaturity of the neural networks leading to imbalances in excitatory and inhibitory amino acids. [30-31] This, in turn, can cause increased excitation or decreased inhibition which, can lead to increased susceptibility to develop seizures. Prior studies comparing the rates of recurrent or late seizures between adults and children also suggest that the mechanisms involved in epileptogenesis in developing and mature brains may be different. These disparities are thought to be due to ontogenic differences in the number, distribution and affinity of the excitatory amino acid receptors. [31]. Further, the long term effects of the increased seizure occurrence in children have not been shown to adversely affect mortality or morbidity in contrast to the findings in adults. [15, 24].

A limitation of this study is that since the relatively rare incidence of stroke in children; [31] we were only able to ascertain 31 childhood strokes despite screening a population of 1.3 million for a total of 24 months in two distinct time periods. Small numbers makes analyses of subgroups difficult. Also the limitations described in prior work with regards to ICD-9 codes and the relatively low yield may underestimate the true incidence. [27]. It is difficult to know the exact time of stroke onset in young children, but assuming that they have close adult supervision in usual circumstances the timing was determined from time the child was last seen as normal. We were unable to discern any undiagnosed cases of status epilepticus presenting as hemiplegia. We are also unable to comment on the rate of subsequent epilepsy in these children,

as our study was designed as an incidence of stroke study and did not have prolonged follow-up of each patient. In addition, we cannot comment on whether seizures occurred before or after noted focal deficits as this was not clearly documented, either in the nursing notes, the physician's notes, or anywhere else in the medical record. Hence, we can only comment on the fact that they occurred or did not occur within a 24 hour period. Hence we report rates of early seizure defined as within 24 hours of noted stroke symptoms. Finally, as with any retrospective study, ascertainment bias may be introduced when using chart review.

Whether seizures in children are more likely to alert a clinician of a possible underlying problem leading to a quicker diagnosis of stroke remains to be determined. Future studies looking at symptoms at presentation and time to make definitive diagnosis of stroke should be considered.

In summary, we found that seizures are quite common in children in the setting of acute stroke. Prior studies have suggested that this presentation may even be more common than hemi paresis or acute motor deficits at presentation .[16, 17, 22]. As acute stroke treatment trials are developed in children, consideration should be made for exclusionary criteria that would be specific to children. If the adult guidelines are used then it is more likely that children would not be eligible for trials. Hence emergency physicians should be aware of this possibly confounding diagnosis. Future studies characterizing acute stroke rates among all patients presenting to emergency departments with new-onset seizures could be helpful in this regard.

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Table 1

Seizure occurrence per stroke subtype.

Type of Stroke	Epileptic seizure	No seizure	Rate of seizure in the acute setting of stroke	P value
N	18	13	58%	
Gender (male)	7 (39%)	9 (46%)		0.68
Race (black)	5 (28%)	4 (31%)		0.86
Age:				0.52
Age (0 -5)years	9 (50%)	4 (31%)	69%	
Age (6-10)years	0 (0%)	3 (23%)	0%	
Age (11-15)years	7 (39%)	3 (23%)	70%	
Age (>16)years	2 (11%)	3 (23%)	40%	
Stroke subtype:				
Infarct	10 (56%)	7 (54%)	59%	
ICH	6 (33%)	6 (46%)	50%	0.53
SAH	2 (11%)	0 (0%)	100%	0.53