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Original Article

Hypertension Is Associated With Increased Mortality in Children Hospitalized With Arterial Ischemic Stroke

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ABSTRACT

BACKGROUND: Recently a single-center study suggested that hypertension after stroke in children was a risk factor for mortality. Our goal was to assess the association between hypertension and outcome after arterial ischemic stroke in children from a large national sample. **METHODS:** Using the Healthcare Cost and Utilization Project Kids' Inpatient Database, children (1-18 years) with a primary diagnosis of ischemic stroke (International Classification of Diseases, Ninth Revision [ICD-9] codes 433-437.1) who also had a diagnosis of elevated blood pressure (ICD-9 code 796.2) or hypertension (ICD-9 codes 401 and 405) from 2003, 2006, and 2009 were identified. Clinical characteristics, discharge outcomes, and length of stay were assessed. Multivariable logistic regression was used to assess the relationship between hypertension and in-hospital mortality or discharge outcomes. **RESULTS:** Of 2590 children admitted with arterial ischemic stroke, 156 (6%) also had a diagnosis of hypertension. Ten percent of children with hypertension also had renal failure. Among patients with arterial ischemic stroke, hypertension was associated with increased mortality (7.4% vs 2.8%; $P = 0.01$) and increased length of stay (mean 11 ± 17 vs 7 ± 12 days; $P = 0.004$) compared with those without hypertension. After adjusting for age, sex, intubation, presence of a fluid and electrolyte disorder, and renal failure, children with hypertension had an increased odds of in-hospital death (odds ratio 1.2, 95% confidence interval [1.1-3.3, $P = 0.04$]). **CONCLUSION:** Hypertension was associated with an increased risk of in-hospital death for children presenting with arterial ischemic stroke. Further prospective study of blood pressure in children with stroke is needed.

Keywords: pediatric stroke, ischemic stroke, hypertension, mortality

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Introduction

Cerebrovascular disorders are among the top ten causes of death in children.[1-3] The incidence of childhood arterial ischemic stroke (AIS) ranges from two to 13 per 100,000 per year in children younger than 18 years in North America and Europe.[3,4] The majority of authors have found an incidence of approximately three per 100,000 children per year.[5]

Hypertension is one of the most important risk factors for stroke in young adults[6] as well as in the elderly but has not been explored in depth in the pediatric literature. Hypertension is present in 1% to 3% of children in the United States.[7-9] The frequency of hypertension discharges rose significantly in children without stroke during 1997 to 2006.[10] The presence of hypertension has been reported in some pediatric stroke studies.[11-14] In one cohort study of children with first AIS, systolic hypertension was found in 104 of 208 patients (50%).[13]

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Elevated blood pressure is common after acute stroke in adults and is associated with poor outcomes at two weeks and six months after stroke; more than half of adults will have a systolic blood pressure reading >160 mm Hg on stroke admission.[15] However, because of the relative infrequency of AIS in children, few publications have addressed outcome after AIS in children with hypertension.[14] One recent single-center study found that of 84 children with acute stroke, 63% had at least one episode of hypertension within the first 3 days after stroke, and hypertension was a risk factor for mortality after stroke.[14] Twenty percent of these children were treated with an antihypertensive medication, a finding that suggests that hypertension was considered clinically significant in at least some patients. However, no studies address the management of poststroke hypertension in children so there are no data to aid pediatric neurologists in answering a common question posed—how blood pressure should be managed after stroke. The objective of this study was to examine the association of hypertension with outcome after AIS in children from a large national sample with the hope that data may provide rationale for future prospective studies.

Methods

The study patient sample was taken from the Kids' Inpatient Database (KID), a part of the Healthcare Cost and Utilization Project (HCUP). A comprehensive synopsis the KID data is available at web site (http://www.hcup-us.ahrq.gov/kidoverview.jsp). KID contains information included in a typical discharge abstract including patient demographics, primary and secondary diagnoses and procedures, discharge status, and length of stay, as well as total hospital charges. For this study we used the KID2003, KID2006, and KID2009.

We used the International Classification of Disease, Ninth Revision, Clinical Modification (ICD-9-CM) primary diagnosis codes 433-437.1 to identify the patients admitted with AIS. ICD-9-CM secondary diagnosis codes were used to identify those with hypertension (401 and 405), elevated blood pressure (796.2), and hypertension comorbidities obtained from the Agency for Healthcare Research and Quality's comorbidity data files. We divided children with AIS into two categories, those with and without hypertension. Study variables included were age; sex; race or ethnicity; and comorbidities obtained from the Agency for Healthcare Research and Quality's co-morbidity data files including diabetes, congestive heart failure, valvular heart disease, peripheral vascular disease, chronic lung disease, fluid and electrolyte disorder, paralysis (as coded in the KID database), deficiency anemia, renal failure, and obesity.

ICD-9-CM secondary diagnosis codes identified secondary diagnoses in children with AIS such as aphasia (784.3), hemiplegia and hemiparesis (342), migraine (346), coma (780.01), moyamoya disease (437.5), seizure (345), congenital heart disease (745-747), altered mental status (780.97), cardiomyopathy (425), systemic lupus erythematosus (710), pneumonia (486, 481, 482.8, and 482.3), sepsis (995.91, 996.64, 038, 995.92, and 999.3), deep venous thrombosis (451.1, 451.2, 451.81, 451.9, 453.1, 453.2, 453.8, and 453.9), intracerebral hemorrhages (431-432), obstructive sleep apnea (327.2), sickle cell disease (282.6), organ transplant (V42.00-V42.90), bone marrow transplant (41.0), and steroid use (99.23). We also used ICD-9-CM primary and secondary procedure codes to estimate the percentage of children who underwent in-hospital procedures such as echocardiography (88.72), computed tomography (87.03), magnetic resonance imaging (88.91), ultrasound imaging of the head and neck (88.71), cerebral angiography (88.41), thrombolytic therapy (99.10), intubation (96.04), mechanical ventilation (96.72), transfusion (99.04), gastrostomy (431.1-431.9), craniotomy (01.24), ventriculostomy placement (02.2), and monitoring for increased intracranial pressure (01.10). If there were <11 discharges for a given variable, that variable was excluded from analysis to avoid biased statistical weighting of small sample sizes as mandated by the use requirements for KID and HCUP policy.

We determined the length of stay, and discharge status was categorized into home, nursing facility, and in-hospital mortality. This study was considered exempt by the institutional review board.

Statistical analysis

SAS 9.3 software (SAS Institute, Cary, NC) was used to convert the KID database data into weighted counts to generate national estimates, following the HCUP recommendations. To identify differences in study variables and end points between children admitted with AIS with and without hypertension, we used χ^2 tests for categorical variables (all variables except age and length of stay) and *t* tests for continuous variables (age and length of stay). Two multivariable logistic regression models were created. Model one included all patients; logistic regression was used to identify the association between hypertension and odds of in-hospital mortality. Model two included only children who survived and were discharged; logistic regression was used to identify the association between hypertension and odds of discharge to a nursing facility. Logistic regression models were adjusted for age, sex, renal failure, fluid and electrolyte disorder, and intubation. A *P*-value of ≤ 0.05 was considered statistically significant.

Results

Of 2590 children age 1 to 18 years with AIS, 156 (6%) had hypertension. Mean age was not different in children with and without hypertension. Hypertension was less common in females (Table 1). Comorbid conditions including fluid and electrolyte disorders, paralysis, and renal failure were all more frequent in those with hypertension than in those without hypertension. Hypertension was more common in children with urinary tract infections. Children with AIS and hypertension also were more likely to have been intubated or to have received mechanical ventilation during their hospital stay.

Hypertension was associated with increased mortality (11 of 156 [7.4%] with hypertension versus 66 of 2434 [2.8%] without hypertension, *P*-value 0.01) and with increased length of stay (11 ± 17 vs 7 ± 12 days; $P = 0.004$) compared with those without hypertension (Table 1). Of the 11 children with hypertension who died, only one had concomitant renal failure.

After adjusting for age, sex, intubation, presence of a fluid and electrolyte disorder, and renal failure, children with hypertension had an increased odds of in-hospital death (odds ratio 1.2, 95% confidence interval [1.1-3.3, $P = 0.04$]) (Table 2). Hypertension was not associated with discharge to a nursing facility versus to the home setting among survivors (Table 2).

Discussion

We examined the association of hypertension with outcome after AIS in children in a large national sample. Hypertension was observed in 6% of children with AIS. We observed higher odds of in-hospital mortality in our study among children with acute stroke and hypertension than in those without hypertension. The association persisted after adjustment for age, sex, intubation, presence of a fluid and electrolyte disorder, and renal failure. In addition, hospital stay was

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