

Trajectories of Outcomes Following Primary Perinatal Hemorrhagic Stroke

Abstract

Background and Objectives: There is a lack of research on perinatal hemorrhagic stroke in term and late preterm infants. Neurological outcomes at two months and two years in a prospective cohort are described.

Methods: Three tertiary pediatric centers took in neonates who were less than 36 weeks pregnant and had a spontaneous parenchymal or intraventricular stroke at less than 28 days of age. Hemorrhagic change of blood vessel ischemic stroke or cerebral sinovenous apoplexy was avoided. The outcomes were evaluated by the Pediatric Stroke Outcome Measure (PSOM). Change over time was evaluated using Wilcoxon signed-rank tests.

Finding: Twenty-six newborns (median age: 1 day, 95% CI 0-16; Age at median gestation: 38.3 weeks, or an IQR of 37.0-39.0). In seven cases, the hemorrhage was isolated intraventricular (27 percent), intraparenchymal (23 percent), or a combination of both. During hospitalization, three newborns (12%) died; one passed away later from heart disease. Results were evaluated at a median of 2.1 months (IQR 1.7-03.3) in 96% of the 22 survivors and 1.9 years (IQR 1.3–2.0) in 73%. The median PSOM scores were, respectively, 0.25 (IQR 0.-1.3) and 0.0 (IQR 0.0-1.0). 45 percent of patients had no or minimal deficits (PSOM 1.0), 30 percent had mild deficits (PSOM 1.0-2.0), and 5 percent had moderate deficits (PSOM 2.5-4.5) at two years. 31% got worse over time and 6% got better. Language sub-scores got worse ($p=0.009$), but total PSOM scores didn't change much ($p=0.08$). None of the children had epilepsy.

Conclusion: Infantile hemorrhagic stroke survivors experienced favorable early childhood outcomes; 5 percent experienced moderate-severe deficits after two years. Language impairments may develop over time and require close monitoring.

Keywords: Perinatal hemorrhagic stroke • Newborn outcomes • Seizure

Introduction

An estimated 1 in 2200-2800 live births have a perinatal stroke, which is a common cause of lifelong neurologic morbidity in late preterm and term infants. The incidence of perinatal hemorrhagic stroke has been reported to be between 1 in 6000 and 9000 live births according to recent data. Although the incidence of perinatal hemorrhagic stroke is comparable to that of perinatal arterial ischemic stroke (1 in 2300-5000 live births), relatively little is known about its risk factors, etiologies, and outcomes. The mechanisms behind late preterm and term hemorrhagic strokes are still a mystery, despite the fact that IVH in premature newborns originates from a fragile germinal matrix. In spite of extensive evaluations over two thirds of cases are consistently described as idiopathic in cohort studies [1].

Methods

Between March 2007 and May 2015, prospective enrollment was conducted at three pediatric tertiary care centers (Johns P. and Monroe Carell Jr. Hospital at Vanderbilt, Children's Hospital of Philadelphia, and Vanderbilt Children's Hospital) for infants born at less than 36 weeks of gestation who presented with a spontaneous hemorrhagic stroke (intraparenchymal or intraventricular hemorrhage) at less than 28 days of age (Center for Children at Hopkins). Computed Tomography (CT) or Magnetic Resonance Imaging (MRI) was used to confirm each

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case. The hemorrhagic transformation of arterial ischemic stroke, cerebral venous sinus thrombosis, or hypoxic ischemic encephalopathy, as well as known trauma, isolated subdural, epidural, or subarachnoid hemorrhage, and hypoxic ischemic encephalopathy were excluded [2].

The prior implementation of a stroke protocol at each institution and the strong relationships between the neurology, neonatology, and neurosurgery departments at all participating institutions helped in the identification of cases. During the initial hospitalization or the infant's first follow up, families were approached for consent and enrollment. Each location received approval from the Institutional Review Board [3].

Determination of outcome

The Pediatric Stroke Outcome Measure (PSOM), a standardized composite score of neurologic function developed for pediatric ischemic stroke and previously utilized in both prospective and retrospective studies of perinatal and pediatric hemorrhagic stroke was used to evaluate outcomes at pediatric stroke clinic visits at two months and two years. Each of the five domains right and left sensorimotor, cognitive/behavioral, expressive and receptive language, and cognitive/behavioral is given a score between 0 and 2, which indicates an increase in the severity of the impairment [4].

After that, domain scores are added together to produce a total score ranging from 0 (no deficit) to 10 (maximum deficit) 14. The outcome status was classified as either "good" if the total PSOM score was less than 1.0, indicating complete recovery or, at most, a mild deficit in a single domain not affecting function, or "poor" if the total PSOM score was less than 1.0 or the patient passed away. Other research teams studying perinatal hemorrhagic stroke¹⁵ have utilized this dichotomy [5].

In order to describe the level of neurologic function, outcomes were also categorized at a more granular level: deficits that do not harm (PSOM 1.0), deficits that are mild (PSOM 1.0-2.0), deficits that are moderate (PSOM 2.5-4.5) and deficits that are severe (PSOM 5.0-10.0, including death). To examine domain specific deficits and their relative trajectories over time, sub-scores were tracked [6].

The right and left sensorimotor sub-scores, as well as the expressive and receptive language sub-scores, were combined for the purpose of analysis, resulting in three sub-score measures:

sensorimotor, cognitive/behavioral, and language together. The use of rehabilitative services and a short survey were also used to assess outcomes qualitatively [7].

Qualitative outcome

At two months or two years, there were no recurrent bleeding episodes. By the two-month follow-up, none of the 22 infants had seizures, but 50% continued to take antiseizure medication (phenobarbital monotherapy in 9/11, levetiracetam immunotherapy in 9/11). Rehabilitative services were being provided to 15 of the 22 infants, or 68 percent. One child had a seizure and a fever at the two-year follow up; every child had stopped taking their daily seizure medication. After a two year follow up, a second child had two seizures and a fever, but remained off antiseizure medication. 44% of parents reported functional impairment in comparison to peers. Two of the 16 children examined at two years used assistive devices, and eight of them (50 percent) continued receiving rehabilitation services [8].

Conclusion

After this above study it was observed that, more than 40% of cases in this prospective cohort study of primary perinatal hemorrhagic stroke were deemed idiopathic. Diatheses with bleeding were the most frequently identified etiology. Even though there was a significant mortality rate of 20%, only 5% of survivors experienced moderate-severe deficits after two years. No child developed epilepsy at a median follow up of two years, and all assessed children had successfully weaned off antiseizure medication. Over time, the total PSOM scores did not change much. However, while sensorimotor and cognitive/behavioral subscores remained stable, language subscores got worse. Overall, these data suggest that deficits may develop over time, particularly in the language domain. In order to better define this population's vulnerability over time and determine the most effective screening and intervention strategy, larger prospective cohort studies of the neurocognitive outcomes of school-aged survivors of primary perinatal hemorrhagic stroke are required [9, 10].

Acknowledgement

None

Conflict of Interest

None

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