Neonatal Stroke Is Not a Harmless Condition

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Neonatal arterial ischemic stroke, defined as a cerebrovascular event occurring between birth and 28 days postnatally with pathological or radiological evidence of focal arterial infarction, is now an increasingly recognized condition. The incidence is commonly referred to as 1/4000 live births.1–4 but higher rates were recently reported.5 Because focal neurological signs of stroke are usually not evident in newborns, there are reasons to believe that the reported incidence of neonatal stroke in a given geographic region is strongly related to the use of neuroradiological techniques. There is now an emerging consensus that all infants with confirmed neonatal seizures should ideally undergo diagnostic neuroimaging to detect ischemic lesions. MRI is clearly the most sensitive technique.6

The etiology of neonatal stroke is not fully elucidated. In only half to three-quarters of cases3,7 can a cause be identified. Major risk factors include prothrombotic disease, congenital heart disease, and perinatal risk factors such as prolonged rupture of membranes and chorioamnionitis.4,8,9 It is interesting to note that neonatal arterial ischemic stroke is related to abnormalities in the coagulation system rather than to fibrinogen activation, as commonly seen in adult stroke. Neonates seem to be at higher risk for stroke than older children,10 which may be because of the fact that pregnancy is a prothrombotic state with a surge of maternal coagulation activation.

Outcome studies to date demonstrate that neonatal stroke has a low mortality and that prognosis is more favorable than for older children and adults,11,12 an effect attributed to plasticity of the immature brain. Impairments after neonatal stroke include hemiparesis, language delay, behavioral problems, and epilepsy.2,13–15

There have been few long-term follow-up studies of cognitive development in children with focal stroke early in life, and results of those studies are disparate. Some report relatively stable intellectual performance for children without epilepsy.16,17 A recent study of 29 preschool to school-age children with documented unilateral ischemic perinatal stroke and 24 controls revealed no evidence of decline in cognitive function with time.18 The study included a subgroup of patients with active epilepsy, and these had adverse cognitive development. Other studies demonstrate a slower rate of cognitive development with time in children with early stroke.19 Many factors may lead to these inconsistent findings. For example, different diagnostic imaging methods (ultrasound, computed tomography, CT, and MRI) and time points for examination were used, patients with both congenital and acquired lesions were included, cross-sectional rather than longitudinal designs were used, control groups were not assessed, and the test–retest interval was short.

In this issue of Stroke, Westmacott and colleagues report a unique study sample on follow-up of children with neonatal unilateral stroke until school age. All cases were extracted from the Children’s Stroke Outcome Study at the Hospital for Sick Children in Toronto and had a history of acute ischemic stroke in the neonatal period with a single unilateral arterial ischemic stroke confined to arterial territories diagnosed by CT or MRI during the first month of life. The clinical indication for imaging was neonatal seizures.

The study was confined to children with focal unilateral lesions without subsequent epilepsy or other comorbidities beyond the neonatal period.

Of the 120 children who met the inclusion/exclusion criteria, only 26 were actually seen twice for follow-up. The excluded group did not differ with regard to motor scores (Pediatric Stroke Outcome Measure [PSOM]), sex ratio, or etiology. Data on socioeconomic status and maternal education were not recorded for the excluded group, why the use of a location-matched control group might have been appropriate.

Twenty-six children were assessed with the age-appropriate Wechsler scales once at preschool age (mean age 4.8 years) and once at school age (mean age 8.9 years). At preschool assessment children with neonatal stroke did not differ from published norms, whereas at school age significantly lower full scales IQ scores, impaired working memory and reduced processing speed compared to the norms were evident. The cognitive weaknesses in children with neonatal stroke were mild in general with a mean full-scale IQ median at school assessment of 94.5, ie, within the normal range. Nevertheless, because there was a decline in full scale IQ, these results underline the importance of long-term follow-up, even for children with normal preschool test results.

As in many neonatal conditions where outcomes in boys are worse than in girls, boys with neonatal stroke had lower scores in cognitive tests than girls (mean full scale IQ 87.6, SD 13.4 versus 97.3, SD 10.89) in the present study. It is interesting to note that these differences were only present at school age, indicating that the male brain may be more at risk for emerging cognitive impairment.

Children with hemiplegia have been noted to have a high risk of cognitive impairments,20 and these difficulties were noted in as many as 25% in a large follow-up study.4 In the present study, 23/26 cases had hemiplegia, indicating that a group of children with severe impairments was studied.
Furthermore, it is known that cognitive abilities may be masked by limitations of movement and motor control in children with cerebral palsy.\textsuperscript{21} Motor function was only assessed using PSOM, which is a potential drawback of the present study. Conversely, no cases were excluded on the basis of motor impairment and PSOM was not related to any of the IQ measures in the present study, and the authors state that motor function was not linearly related to cognitive outcome.

All infants diagnosed with arterial ischemic stroke in the present study had porencephaly. This, and the mentioned high proportion of hemiplegia in the sample, indicates that a group with severe focal injury had been selected. It is therefore not necessarily so that a group of children with more restricted focal injury would exhibit similar decline in cognitive testing.

Nevertheless, stroke to the developing brain may have been underestimated in terms of incidence and, as shown in the study by Westmacott and colleagues, in terms of consequences. It is conceivable that early injury to the brain affects the development of neuronal pathways and that functional impairments develop with time. The major conclusion from their study is that the majority of children with unilateral neonatal stroke show declines in several cognitive domains, thereby emphasizing the importance of long-term follow-up of this group of patients.

Disclosures

None.

References

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Stroke. 2009;40:1948-1949; originally published online May 7, 2009;
doi: 10.1161/STROKEAHA.109.550152
Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0039-2499. Online ISSN: 1524-4628

The online version of this article, along with updated information and services, is located on the
World Wide Web at:
http://stroke.ahajournals.org/content/40/6/1948

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