EDITORIAL

An Extended Way to Predict Neonatal Hypoxic Ischemic Encephalopathy

Globally, hypoxic ischemic encephalopathy (HIE) is the leading cause of neonatal brain injury. Before the introduction of neuroprotective therapy with moderate hypothermia, children with acute perinatal and/or neonatal HIE having moderate encephalopathy had disability rates of 6–21%; however, in those with severe encephalopathy, this rate was even higher (42–100%). Thus, it is very important to evaluate the severity of central nervous system injury and neurological outcome in neonatal HIE cases to determine possible treatment options and counsel parents.

Two pilot, prospective studies in the United Kingdom (TOBY Study Group) and in the United States (NICHD Neonatal Research Network) reported a similar conclusion that moderate hypothermia resulted in lower death rates and seemed to improve neurocognitive outcomes in children with moderate to severe neonatal HIE.

To date, the condition of the infant at birth, the severity of HIE, and neurophysiological tests, including amplitude-integrated electroencephalography and biomarkers (e.g., serum S100 and neuron-specific enolase), and neuroimaging have been used to evaluate prognosis and predict long-term outcome. However, these indicators seemed to have only modest predictive accuracy. "Do we actually realize the pathologic mechanisms of neonatal HIE, for example, the role of TNFR1-JNK signaling in neonatal HIE?" Such knowledge will provide additional information for utilization of suitable biomarkers and improve clinical outcomes.

Magnetic resonance imaging (MRI) is the most helpful method to predict neurological outcomes in infants in their initial stages of birth. However, it is difficult to conduct an MRI within the first 24–48 hours after birth in infants with moderate to severe HIE having unstable vital signs (e.g., postneonatal asphyxia) and/or while receiving moderate hypothermia therapy due to clinical difficulties.

Interestingly, an applicable predictive method for moderate to severe neonatal HIE has been published in Pediatrics and Neonatology by Nanavati et al in which continuous electroencephalography (EEG) monitoring was obtained for 72 hours and EEG findings were evaluated at 24 hours and 72 hours in combination with brain MRI obtained within 1 week after birth. The authors of that study demonstrated a statistically significant rank correlation between the EEG and MRI scores at 72 hours (p = 0.012). Likewise, they also revealed a statistically significant relationship between MRI and the clinical outcome (p = 0.0174). MRI obtained at 72 hours of life demonstrated the following: positive predictive value of 1, negative predictive value of 0.83, with sensitivity and specificity of 100% and 83%, respectively. However, only the EEG severity scale at 24 hours and clinical outcome showed a statistically significant relationship (p = 0.024); there was no significant relationship between EEG findings at 72 hours and clinical outcome. This discrepancy in EEG findings obtained at 24 hours and 72 hours since birth may be due to the effect of hypothermia and the improvement in neuroplasticity in newborns.

However, this study has some limitations, which are as follows. (1) Only 17 neonates with moderate to severe HIE were enrolled. (2) The study design was retrospective. For stronger evidence, a prospective study should be analyzed in the future. (3) The study did not include any infants with mild to moderate HIE. Studying such cases would have enabled to follow their outcomes post-treatment and compare their outcomes with those of infants with moderate to severe HIE.

In summary, despite continued progress in treatment modalities, accurate prediction of neonatal HIE remains a challenge. "Do we have the consensus to score the severity of EEG and MRI in comparison with clinical presentations and functional outcomes of neonates with HIE?" Nanavati et al tried to predict neurocognitive outcomes in neonates with HIE using a combination of brain MRI and EEG and the data presented are encouraging. Various studies are being carried out to identify tools for accurately predicting neonatal HIE, and this interesting article adds to this growing body of research.
Conflicts of interest

The author reports no conflict of interest.

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