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Original Article

The Correlation Between a Short-term Conventional Electroencephalography in the First Day of Life and Brain Magnetic Resonance Imaging in Newborns Undergoing Hypothermia for Hypoxic-Ischemic Encephalopathy

Rawad Obeid MD [a,*], Yoshimi Sogawa MD [b,], Satyanarayana Gedela MD [b,1], Monica Naik MD [b], Vince Lee PhD [c], Richard Telesco MD [d], Jessica Wisnowski PhD [e], Christine Magill PA-C [b,2], Michael J. Painter MD [b], Ashok Panigrahy MD [c]**

[a] *Department of Neurology, Children's National Health System, Washington, District of Columbia*
[b] *Division of Pediatric Neurology, Children's Hospital of Pittsburgh, Pittsburgh, Pennsylvania*
[c] *Division of Pediatric Radiology, Children's Hospital of Pittsburgh, Pittsburgh, Pennsylvania*
[d] *Division of Newborn Medicine, Children's Hospital of Pittsburgh, Pittsburgh, Pennsylvania*
[e] *Department of Radiology, Children's Hospital of Los Angeles, Los Angeles, California*

ABSTRACT

OBJECTIVE: Electroencephalograph recorded in the first day of life in newborns treated with hypothermia for hypoxic-ischemic encephalopathy could be utilized as a predictive tool for the severity of brain injury on magnetic resonance imaging and mortality. **STUDY DESIGN:** We analyzed newborns who were admitted for therapeutic hypothermia due to hypoxic-ischemic encephalopathy. All enrolled infants underwent encephalography within the first 24 hours of life and underwent brain magnetic resonance imaging after rewarming. All encephalographs were independently reviewed for background amplitude, continuity, and variability. Brain injury determined by magnetic resonance imaging was scored using methods described by Bonifacio et al. **RESULTS:** Forty-one newborns were included in the study. Each encephalograph variable correlated significantly with the severity of injury on brain magnetic resonance imaging ($P < 0.001$ for each). The overall encephalograph severity estimated as mild, moderate, and severe also correlated with injury ($P < 0.001$). Each encephalograph variable correlated with mortality ($P < 0.001$ for each) and also the overall encephalograph severity ($P < 0.001$). **CONCLUSION:** Severity of electrographic findings on encephalograph in the first day of life during therapeutic hypothermia for hypoxic-ischemic encephalopathy correlated with the extent of injury on brain magnetic resonance imaging. This information may be useful for families and aid guide clinical decision making.

Keywords: HIE, newborns, EEG, MRI, neuroprotection, neonatal intensive care, whole body cooling

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Introduction

Hypoxic-ischemic encephalopathy (HIE) is a common cause of neonatal brain injury resulting in significant morbidity and mortality.[1] Early estimation of brain injury after HIE is important for planning treatment and to counsel parents. Clinically, the most widely utilized measure to characterize neurological functioning in newborns with HIE is the Sarnat staging, which relies largely on neurological examination.[2] The prognostic utility of this staging method requires serial examinations for 72 hours after the hypoxic

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* Communications should be addressed to: Dr. Obeid; Children's National Health Center; Department of Neurology and Center of Neuroscience Research; 111 Michigan Avenue, NW; Washington, DC, 20010.

** Dr. Sogawa; The Children's Hospital of Pittsburgh of UPMC; 4401 Penn Avenue; Pittsburgh, PA, 15224.

E-mail addresses: rawad.obeid@hotmail.com; yoshimi.sogawa@chp.edu

[1]Dr. Gedela current address: Division of Pediatric Neurology, Nationwide Children's Hospital, 700 Children's Drive, Columbus, OH 43205.

[2]Miss Magill current address: Brigham and Women's Hospital, 75 Francis St., Boston, MA 02115.

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TABLE 1.
Electroencephalograph (EEG) Ordinal Variables

Degree of Abnormality	EEG Variables		
	Background Amplitude	Continuity	Variability
Mildly abnormal	>25 μV	Continuous >50% of the recording	Clear sleep–wake cycle
Moderately abnormal	5-25 μV	Discontinuous >50% of the recording with interburst intervals ≤20 seconds	Inconsistent sleep–wake cycles
Severely abnormal	<5 μV	Discontinuous >50% of the recording with interburst intervals >20 seconds	No variability

event.[3] The staging method has limited value for estimating the extent of cerebral injury in the first 24 hours of life. In contrast, magnetic resonance imaging (MRI) has been shown to be highly reliable for demonstrating injury in newborns with HIE and is highly predictive of outcome.[4-8] Its utility for early evaluation of brain injury, however, is hampered by the technical challenges associated with obtaining MRI during therapeutic hypothermia and the lack of sensitivity in the first 24 hours of life.[9]

Electroencephalography (EEG) has long been used to provide prognostic information in newborns with HIE.[10-18] It is widely available in most pediatric hospitals and compatible with hypothermia protocols. EEG is a well-established clinical standard for diagnosing seizures[19-21] and predicting brain injury when done as continuous long-term recording after the event.[22-24] There are limited data, however, on the utility of a short-term recording for predicting brain injury in newborns with HIE on the first day of life.

Given the need to determine prognosis earlier in the course of HIE in order to make therapeutic decisions, the aim of our study was to evaluate the utility of a one-hour EEG carried out within the first 24 hours after birth. Specifically we were interested in determining whether short-term EEG monitoring could aid in the prediction of the severity of brain injury visualized on MRI, and could be related to early mortality.

Method/Study design

We retrospectively examined medical records and identified all newborns who were treated with therapeutic hypothermia for neonatal HIE at Magee Women's Hospital and the Children's Hospital of Pittsburgh between June 2011 and December 2013. The approval of the University of Pittsburgh Review Board was obtained before beginning the study.

As per institutional protocol, newborn infants were cooled to 33.5°C using a servo-controlled device (Criticool, Vital Care Products, Inc, Richfield, OH) if the following criteria were present: gestational age 36 weeks or more, birth weight 1800 grams or less, age less than six hours, no major congenital or known chromosomal anomalies, no immediate plan to redirect care, moderate to severe HIE based on a modified Sarnat criteria used in the National Institute of Child Health and Human Development Neonatal Research Network (NICHD) trial,[25] and laboratory evidence of hypoxia-ischemia at birth defined as blood gases before one one hour of life (either umbilical cord, arterial, or venous blood) with pH less than 7.00 and a base deficit greater than 16 mEq/L. In the absence of laboratory evidence of hypoxia-ischemia at birth, the newborn must have all the following: ten minute Apgar score ≤5, continued resuscitation or ventilation for ten or more minutes after birth, and an identified acute perinatal event (e.g., severe late or variable deceleration, cord prolapse, cord rupture, placental abruption, uterine rupture, maternal trauma, maternal arrest, maternal seizure).

Of importance, at both Magee Women's Hospital and Children's Hospital of Pittsburgh, our clinical protocol for therapeutic hypothermia includes a minimum of one hour-long EEG, which is typically obtained within the first 24 hours of life. The duration of the EEG recording could be extended up to several days (continuous EEG) based on clinical judgment. Mortality information occurring during the first week of life was obtained from the medical records.

Electroencephalography

All EEGs were recorded during cooling to 33.5°C measured by a rectal probe within the first 24 hours of life. International 10/20 system of electrodes placement modified for neonates was applied, with concomitant electrocardiogram, eye, respiratory, and chin leads.

The EEG was recorded on Bio-Logic machines with either Natus (version 7.1.1) or Ceegraph (version 7.03.04) software. Two board-certified pediatric electrophysiologists (Y.S. and S.G.) blinded to any clinical information, except for the adjusted gestational age, reviewed all EEGs independently. Before this study, the readers reviewed five unrelated neonatal EEGs to standardize and define EEG criteria. In case of discrepancy in EEG scoring, a consensus reading was reached. EEG findings were recorded on a standardized form based on published data[26-30] and including ordinal variables, which were categorized according to the degree of abnormality (Table 1). The EEG was evaluated using a bipolar anterior-posterior montage with sensitivity of 5 μV and a speed of 20 seconds per page. The dominant amplitude was measured over C3–O1 and C4–O2 leads during artifact-free ten seconds epoch for several times then averaged. We evaluated the ordinal variables independently, and then combined in an EEG scale (mild, moderate, and severe). Mildly abnormal EEG was defined by background amplitude of ≥25 mV with continuous activity for greater than 50% of the recording, and the presence of sleep–wake cycling. Moderately abnormal EEG was assigned to EEG findings that did not clearly meet the mild or severe parameters. Severely abnormal EEG was defined by background activity of less than 5 mV with discontinuity greater than 20 seconds interburst interval (IBI) for more than 50% of the recording and no variability. The variability on EEG was documented in the case of state change or clear sleep–wake cycling during the recording and without stimulating procedures. Additionally, we defined the presence of electrographic seizures on EEG as a ten second rhythmic electrical discharge. Some of the newborns received antiepilepsy medications within a few hours after birth for movements that were suspicious for seizure. This typically happened in newborns who were transferred from other hospitals after birth. Examples of EEG continuity and discontinuity are available in Fig. 1.

Brain MRI

Per institutional protocol, newborns with HIE who survive therapeutic hypothermia undergo a brain MRI as soon as possible following rewarming (typically day of life four to five). All brain MRIs were conducted on a GE MR system (Signa LX operating at 1.5T or 3T; GE Healthcare, Milwaukee, WI) using a customized neonatal