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Amplitude-Integrated EEG and Cerebral Near-Infrared Spectroscopy in Cooled, Asphyxiated Infants

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Abstract

Objective To assess the predictive value of amplitude-integrated electroencephalography EEG (aEEG) and near-infrared spectroscopy (NIRS) during therapeutic hypothermia.

Patients and Methods We studied 39 cooled, asphyxiated infants. We assessed aEEG and calculated mean regional cerebral oxygen saturation (rcSO₂) during and after treatment. At 30 months, we performed a neurological examination and administered the Bayley Scales of Infant and Toddler Development, 3rd edition. We calculated the odds ratios (ORs) of abnormal aEEG and rcSO₂ for severely abnormal outcome.

Results At 6 and 12 hours, severely abnormal aEEGs predicted severely abnormal outcomes (OR, 7.7 [95% confidence interval, CI, 1.39–42.6] and 24.4 [95% CI 4.2–143] respectively), as did epileptic activity (OR 28.9, 4.6–183). During the first 48 hours, rcSO₂ was not associated with outcome, but at 72 hours after birth and after rewarming it was, with ORs for severely abnormal outcomes of 12.8 (1.31–124) and 21.6 (1.05–189), respectively. In multivariate analyses, aEEG and rcSO₂ remained independently predictive in the model at 48 hours and significantly from 72 hours after birth onward.

Conclusion aEEG was a strong predictor of adverse outcome. After 48 hours of cooling, a higher rcSO₂ was associated with a severely abnormal outcome, adding to the predictive value of aEEG in cooled, asphyxiated infants.

Keywords

- aEEG
- NIRS
- MRI
- therapeutic hypothermia
- asphyxia
- newborns

Hypoxic-ischemic encephalopathy (HIE) due to perinatal asphyxia is among the most frequent causes of brain damage in full-term neonates. Twenty to thirty percent of infants with cerebral palsy (CP) suffered HIE. The incidence of HIE has not changed over the last 40 years.¹ Brain damage following HIE results from multiple processes including deposition of calcium in the damaged neurons, cerebral edema, necrosis and apoptosis of neurons, and activation

of microglia.² In full-term newborns, therapeutic hypothermia (TH) treatment started within 6 hours after birth has proved to protect against such brain damage.^{3–5} In 2009, TH was introduced at our unit as a standard treatment in full-term newborns (gestational age > 36 weeks) with HIE.

Various techniques are used to assess brain function in infants with HIE. In the precooling era, due to it being highly predictive of neurological outcome, amplitude-integrated

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electroencephalography (aEEG) was considered an accurate tool to assess brain function in asphyxiated full-term newborns.^{6–8} In the current cooling era, however, it has been reported that aEEG background patterns recover more slowly, and that sleep–wake cycling starts later during TH.⁹ Therefore, the value of using aEEG as an early outcome predictive tool during TH treatment in infants with HIE seems limited.^{9–11}

A tool that might help us predict the outcome of asphyxiated infants undergoing TH treatment more accurately is near infrared spectroscopy (NIRS). It measures regional cerebral oxygen saturation (rcSO₂). Data on the predictive value of NIRS in cooled newborns with HIE suggest that rcSO₂ values are higher in infants with adverse outcomes, as a result of lower cerebral metabolism.^{12,13} However, the exact time course of rcSO₂ values during cooling has not been elucidated, and little data exists on rcSO₂ after rewarming. In several studies, aEEG and NIRS data have been collected, but both were analyzed separately in relation to outcome. Furthermore, the predictive value of the combination of aEEG and NIRS has hardly been studied.

Therefore, the aim of this study was to determine the predictive value of aEEG and NIRS alone, and in combination, during the first 4 days after perinatal asphyxia, in full-term and in nearly full-term newborns undergoing TH treatment for HIE.

Patients and Methods

Study Population

This retrospective pilot study was performed at the neonatal intensive care unit of the University Medical Center Groningen, the Netherlands. Using our medical database, we identified all infants who had been admitted with HIE between May 2009 and January 2011 and who had undergone TH treatment. In our unit, recording aEEGs is a routine procedure in all critically ill infants. In addition, we monitor cerebral oxygenation by using NIRS.

Perinatal asphyxia was defined as Apgar scores of 5 or less at 5 minutes, resuscitation/artificial ventilation for > 10 minutes, umbilical cord pH of < 7.0 and base deficit of > 16 mmol/L, or lactate of > 10.0 mmol/L. The level of HIE was scored by the attending neonatologist, using the Thompson score. A score of 7 or more was considered as moderate-to-severe HIE and was used as the cut-off value for starting TH treatment. In case of a lower Thompson score (≤ 7) but an abnormal aEEG background pattern (discontinuous normal voltage, DNV), cooling was also initiated. We used the CritiCool (Charter Kontron, Milton Keynes, United Kingdom) to provide total body hypothermia, aiming at a core temperature of 33.5°C for 72 hours. Rewarming commenced after 72 hours at a rate of 0.4°C/h. During cooling, infants were routinely sedated with morphine (10 µg/kg/h). Midazolam (loading 0.05 mg/kg, maintenance 0.1 mg/kg/h) was added if sedation was inadequate. Seizures were treated according to local protocol with phenobarbitone (maximum 40 mg/kg) being the drug of first choice, and midazolam and lidocaine being the drug of second and third choice, respectively.

Between May 2009 and January 2011, a total of 42 infants had undergone TH treatment. We excluded three infants with congenital anomalies not yet obvious at the time treatment commenced. One of the three infants had CHARGE syndrome, one had trisomy 18, and the third had a 22-q-11 deletion. Treatment started at a mean postnatal age of 4 hours and 34 minutes. Because we offered passive cooling during transportation shortly after the introduction of TH, the majority of infants had already been cooled to some extent at an even earlier postnatal age. Twenty-four (62%) of the infants had a core temperature below 35.0°C on admission.

We obtained the infants' clinical information from their medical records. This included Apgar scores, gestational age, birth weight, circulatory and respiratory parameters, umbilical cord pH, lactate level, the presence of multiorgan failure, and the presence of clinical seizures. Magnetic resonance imaging (MRI) was performed at a median postnatal age of 6 days (range 4–13). MRI sequences were assessed for cortical injury in watershed areas, injury to the basal ganglia, and myelin signal in the posterior limb of the internal capsule by using the scoring method developed by van Rooij et al.¹⁴ More pathology led to a higher score. A total score of < 4 points was considered mildly abnormal, whereas a score of ≥ 4 was considered severely abnormal. The cut-off at 4 was chosen in accordance with the median MRI scores in the article by van Rooij et al.¹⁴

The study was approved by the medical ethics review board of University Medical Center Groningen.

Assessment of the aEEG Recordings

The aEEGs were recorded by either one of two cerebral function monitors: Olympic CFM 6000 (Natus Medical Inc, Pleasanton, CA) or the analog Lectromed Multitrace 2 (Lectromed, United Kingdom). In 95% of cases, the Olympic CFM 6000 was used. If the Lectromed Multitrace 2 monitor was used, it was calibrated every 24 hours. Biparietal needle electrodes (P3 and P4, according to the international 10–20 system of electrode placement) were used for the recordings. During each recording, we took care that the impedance was < 5 kΩ. The nursing staff recorded all nursing and medical procedures, clinical seizures, as well as all medication administered.

We analyzed the aEEG recordings made during TH treatment at 6, 12, 24, 48, and 72 hours after birth, and at 24 hours after rewarming. For the assessment, we used an epoch of 1 hour around the targeted time. We assessed the aEEG recordings by pattern recognition. All traces were assessed by one senior neonatologist (HtH) blinded to the severity of the HIE. The aEEG background patterns, epileptic activity (EA), and the presence of sleep–wake cycling (SWC) were assessed. We confirmed EA by analyzing the simultaneously recorded, single-lead EEG, or by intermittent conventional EEG in case of Lectromed traces, if EA was suspected. We classified the different aEEG background patterns as continuous normal voltage (CNV), DNV, burst suppression (BS), continuous low voltage (CLV), or flat trace (FT), according to the criteria established by Toet et al.⁷ We considered CNV to be a normal background pattern and DNV as a mildly abnormal. The low voltage traces, BS, CLV, and FT, we considered as severely abnormal.

We classified EA as a single seizure in case of a single event of sudden, sustained high cortical activity; as repetitive seizures in case of repetitive events of sudden, sustained high cortical activity, and as status epilepticus in case of repeated EA resulting in a regular pattern of increased cortical activity (saw-tooth pattern) lasting for > 50% of a 1 hour epoch.

We identified SWC by the altered width of the amplitude of the tracing indicating different, alternating sleep stages.

Near-Infrared Spectroscopy Recordings

We recorded rcSO₂ continuously during TH treatment and rewarming, and used the INVOS 5100C (Somanetics Corporation, Troy, MI) with the pediatric sensor. Dix et al¹⁵ found that the neonatal and pediatric sensors gave similar regional tissue saturation values. In comparison to the adult sensor, rcSO₂ values measured with the pediatric or neonatal sensor are approximately 10% higher.¹⁵

We placed the NIRS sensor on the left or right frontoparietal side of the infant's head and it was held in position by an adhesive bandage to prevent the sensor from slipping. A mean rcSO₂ was calculated over a 1-hour period at 6, 12, 24, 48, 72 hours after birth, and 24 hours after rewarming.

Long-Term Follow-Up

Follow-up at the age of 30 months consisted of a neurological examination according to Touwen's method,¹⁶ on the basis of which we determined the presence of CP. This condition was further categorized according to the Gross Motor Function Classification System (GMFCS).¹⁷ Additionally, we assessed cognitive outcome and motor development by using the Bayley Scale of Infant and Toddler Development, 3rd edition (BSID-III). Using the results of both the neurological examination and the BSID-III, we classified the children as normal in the absence of CP and/or a BSID-III score of ≥ 85, mildly abnormal if there was a CP with a GMFCS 1 or 2 and/or a BSID-III score between 70 and 85, and severely abnormal in case of death, a BSID-III score of < 70 and/or a CP with a GMFCS score of ≥ 3. For further analyses, we combined the mildly abnormal with the normal group.

Statistical Analysis

We used SPSS software for Windows, version 20.0 (SPSS Inc. Chicago, IL) for all the analyses. To test the relationship between aEEG background patterns and rcSO₂ values, we performed a one-way analysis of variance. Cut-off values of rcSO₂ for the prediction of a severely abnormal outcome were investigated with receiver operating characteristics (ROC) analyses. For every time point and by using univariate analyses, we assessed the differences regarding aEEG characteristics and rcSO₂ values between infants with good and severely abnormal outcomes. The tests included the Mann Whitney U test and univariate logistic regression analyses. We calculated the odds ratios (ORs), including 95% confidence intervals (CIs) of the aEEG traces and rcSO₂ values for a severely abnormal outcome. Next, we performed multiple logistic regression analyses entering aEEG and rcSO₂ in the model (method backward), to assess which factor contrib-

uted independently to the prediction of the outcome. Statistical significance was defined as *p* < 0.05.

Results

Patient Characteristics

The patient characteristics are shown in ►Table 1. Twelve infants died during the course of the study: four infants died during hypothermia and eight infants died after rewarming. Of the 27 surviving infants, outcome was normal in 25 infants (two parents refused that their infants participated in testing with BSID-III, but both had normal neurologic and pediatric exams), mildly abnormal in one infant, and severely abnormal outcome in another. This latter infant had CP with a GMFCS-level above 2.

Of the infants with a MRI score ≥ 4, two infants survived with a normal outcome. In eight infants that died after the cooling period, we performed a MRI at a mean age of 5.4 days (range 4–8). MRI scores were severely abnormal (≥ 4 according to van Rooij et al¹⁴) in 75% of the infants with a mean score of 4.9 (range 3–8).

Time Course of aEEG

The distribution of infants with normal and abnormal aEEG patterns during cooling and after rewarming is presented in ►Table 2. At certain time points, some infants had died and others had unreliable aEEG readings. The majority of infants

Table 1 Patient characteristics (N = 39)

Gestational age, wk	39.7 (37–42.1)
Birth weight, g	3437 (2350–915)
Apgar score at 1 minute, median (range)	1 (0–7)
Apgar score at 5 minute, median (range)	3 (0–7)
Apgar score at 10 minute, median (range)	4 (0–8)
First arterial blood gas pH ^a	7.24 (6.47–7.50)
First arterial blood gas BE ^a	-11,8 (-31,7–1,2)
pH umbilical	6.93 (6.64–7.28)
Lactate, mmol/L	12.1 (1.9–24)
Base excess, mEq/L	-18.4 (-34–0.3)
Start hypothermia, h	4:33 (0:45–6:22)
Thompson score, median (range)	10 (6–18)
Death, <i>n</i> (%)	12 (31)
MRI score ^b	
0 (normal)	9 (26)
≥ 1 and ≤ 3	18 (51)
≥ 4	8 (23)

Abbreviation: MRI, magnetic resonance imaging.
Data are given as mean (range) unless otherwise described.
^aAt a mean postnatal age of 5.7 hours (0.5–12.5).
^bMRI score according to the method by van Rooij et al.¹⁴

Table 2 Distribution of infants with normal and abnormal aEEG background patterns during hypothermia and after rewarming

PNA (h)	CNV	DNV	BS	CLV	FT	n	Died
6	6 (16)	10 (27)	15 (41)	none	6 (16)	37	None
12	10 (26)	15 (40)	3 (8)	3 (8)	7 (18)	38	None
24	9 (24)	14 (37)	5 (13)	7 (18)	3 (8)	38	None
48	11 (31)	14 (39)	3 (8)	4 (11)	4 (11)	36	1
72	11 (34)	13 (41)	6 (19)	2 (6)	none	32	4
24 h after rewarming	22 (67)	5 (15)	5 (15)	1 (3)	none	33	6

Abbreviations: aEEG amplitude integrated EEG; BS, burst suppression; CLV, continuous low voltage; CNV, continuous normal voltage; DNV, discontinuous normal voltage; FT, flat trace; PNA, postnatal age.

Note: Data are presented as numbers (%).

(84%) had a mildly or severely abnormal aEEG at 6 hours after birth and 57% of infants had a severely abnormal aEEG. Within the first 12 hours following birth, the percentage of severely abnormal background patterns decreased. After these first 12 hours following birth, the total number with CNV or DNV more or less stayed the same. SWC were present in 24 infants (median 50 hours). EA was present in 15 infants (38%).

Time Course of NIRS

During TH, $rcSO_2$ increased with increasing postnatal age. It increased from 71% (interquartile range, IQR, 65–75) at 6 hours postnatal age to 82% (IQR 78–90) at 24 hours ($p = 0.001$), 88% (IQR 86–94) at 48 hours ($p < 0.001$), and 87% (IQR 81–94) at 72 hours ($p < 0.001$). After rewarming, $rcSO_2$ decreased to 83% at 24 hours (IQR 77–92). Abnormal $rcSO_2$ values were present in 27% of the infants at 6 hours postnatal age. These values increased to 62% at 48 hours postnatal age, and decreased to 44% at 72 hours postnatal age (► **Table 3**).

Prognostic Value of aEEG

Infants with abnormal aEEG background patterns more often had a severely abnormal outcome, whereas infants with normal or mildly abnormal aEEG background patterns more often had normal outcomes (► **Table 4**). Severely abnormal background patterns had a high OR for a severely abnormal outcome during the entire cooling period and after rewarming (► **Table 4**). Eleven infants had a severely abnormal aEEG at 48 hours (► **Table 2**). Two of these infants had a good outcome. SWC appeared in only one out of 13 infants

with severely abnormal outcomes (8%) and in 23 out of 26 (88%) infants with normal outcomes. This resulted in an OR of the absence of SWC for a severely abnormal outcome of 138.0 (95% CI 11.3–1681, $p < 0.001$).

EA, often presenting within the first 24 hours, was more frequent in infants with severely abnormal outcomes (85%) when compared with infants with normal outcomes (16%) with an OR for a severely abnormal outcome of 28.9 (95% CI 4.6–183, $p = 0.001$). We found no difference between single seizures or repetitive seizures in relation to outcome.

Predictive Value of NIRS

The ROC curves of $rcSO_2$ at 48 hours after birth, 72 hours after birth, and following rewarming illustrated that an $rcSO_2 \geq 90\%$ was predictive for a severely abnormal outcome. At 48 hours, a $rcSO_2 \geq 90\%$ had a sensitivity of 88% and a specificity of 50%, with area under the curve (AUC) of 0.78 (95% CI 0.57–0.99, $p = 0.022$) for prediction of a severely abnormal outcome. At 72 hours, the sensitivity and specificity were 86% and 68%, respectively, with AUC of 0.81 (95% CI 0.57–1.0, $p = 0.013$) and after rewarming the sensitivity and specificity were 86% and 82%, respectively, with AUC 0.90 (95% CI 0.77–1.0, $p = 0.013$).

During the first 48 hours of TH, $rcSO_2$ was not significantly different between the infants who survived and those who died. In comparison to infants with normal outcomes, infants with severely abnormal outcomes had higher $rcSO_2$ values at 72 hours postnatal age (median 95% vs 86%, $p = 0.037$) and at 24 hours after rewarming (median 94% vs 79%, $p = 0.003$) (► **Fig. 1**). The ORs of $rcSO_2$ defined as normal or abnormal for

Table 3 Distribution of infants according to their $rcSO_2$ values during therapeutic hypothermia and after rewarming

PNA (h)	$rcSO_2 \leq 65\%$	$rcSO_2 66\text{--}89\%$	$rcSO_2 \geq 90\%$	n	Died
6	6 (20)	22 (73)	2 (7)	30	None
12	5 (14)	27 (77)	3 (9)	35	None
24	2 (6)	24 (73)	7 (21)	33	None
48	None	10 (38)	16 (62)	26	1
72	None	18 (56)	14 (44)	32	4
24 h after rewarming	None	19 (63)	11 (37)	30	6

Abbreviations: PNA, postnatal age; $rcSO_2$ indicates regional cerebral oxygen saturation. Data are presented as numbers (%).

Table 4 ORs and 95% CI for severely abnormal outcome, regarding abnormal aEEG background patterns and abnormal rcSO₂ values in both univariate and backward multiple regression models

PNA (h)	aEEG background pattern (A vs. N) OR (95% CI)	R ² (%)	p-Value	Multivariate logistic regression (METHOD backward)		
				aEEG background pattern (A vs. N) OR (95% CI); p-Value	rcSO ₂ (A vs. N) OR (95% CI); p-Value	R ² (%)
6	7.7 (1.39–42.6)	23.3	0.019	4.44 (0.74–26.7) 0.10	Not in the model	13.7
12	24.4 (4.2–143)	48.5	< 0.001	16.3 (2.7–100) 0.003	Not in the model	39.0
24	13.3 (2.6–67.4)	37.2	0.002	8.9 (1.67–47.2) 0.011	Not in the model	27.7
48	14.0 (2.6–80.0)	36.4	0.002	10.9 (0.99–120) 0.051	13.5 (0.89–204) 0.060	38.6
72	11.7 (1.79–79.0)	30.3	0.010	12.1 (1.02–143) 0.048	18.0 (1.28–254) 0.032	49.6
24 h after rewarming	19.2 (2.5–147)	37.6	0.004	Not in the model	25.5 (2.36–275) 0.008	45.6

Abbreviations: A, abnormal; aEEG, amplitude integrated EEG; CI, confidence interval; N, normal; OR, odds ratio; PNA, postnatal age; rcSO₂, regional cerebral oxygen saturation. Note: LR+ and LR- (95% CI).

Fig. 1 Time course of rcSO₂ during hypothermia and after rewarming in relation to outcome. □ normal or mildly abnormal; ■ severely abnormal or death; RW24, 24 hours after rewarming; * *p* < 0.05; ** *p* < 0.01.

adverse outcomes were 12.8 (95% CI 1.31–124) at 72 hours postnatal age and 27.0 (95% CI 2.5–291) 24 hours after rewarming (► Table 4).

The Combined Predictive Value of NIRS and aEEG

We found no relationship between the aEEG background pattern and rcSO₂ values. We performed multiple logistic regression analyses to evaluate the combined predictive value of NIRS and aEEG (► Table 4). At 48 hours and 72 hours after birth, both rcSO₂ and aEEG remained in the model, at 48 hours with concomitant *p* values just above 0.05, explaining 38.6% of the variance. At 72 hours, the explained variance was 49.6%. After rewarming, only rcSO₂ remained in the model.

Discussion

In the present study, we found that aEEG is a powerful predictive tool, also during TH treatment. During the first 48 hours after birth, cerebral oxygen saturation, measured by using NIRS, provided little additional information. However, 72 hours after birth and particularly after rewarming, rcSO₂ contributed substantially toward predicting an infant's outcome. In infants with severely abnormal outcomes, including death, rcSO₂ values remained high in comparison to the values in infants with normal or mildly abnormal outcomes.

The lower predictive value of aEEG is in line with other studies investigating the effect of TH on aEEG.^{9–11} Studies that were performed in the precooling era pointed out that the predictive value of aEEG increased with increasing postnatal age, with the highest accuracy at 12 to 24 hours after birth.^{6,18} The predictive value of aEEG during TH treatment is acquired at a later postnatal age than in the precooling area, that is, mostly after 48 hours.^{9,19,20} This may be explained by the lower level of cerebral activity during TH, or it may be caused by the sedative drugs that were administered during

TH. We were, however, unable to confirm the highest predictive values at or after 48 hours in our study because the aEEG background patterns were already highly predictive at 12 hours after birth. These high predictive values continued during the entire cooling procedure and after rewarming, an observation which is in line with findings of previous studies regarding aEEG in cooled infants. That we already found high predictive values of aEEG background patterns at 12 hours might be a chance finding, because the predictive values were lower after this initial high value.

SWC is considered to reflect the integrity of the brain. Our study confirms that the presence of SWC and early onset of SWC during cooling are predictive of a favorable outcome. This is in accordance with other studies which reported that the presence of SWC was more frequent and that it emerged sooner in noncooled infants with favorable outcomes than in infants with poor outcomes.^{21–23} This has also been reported in the case of cooled infants.¹⁹

Absence of EA during cooling was also highly predictive of good outcomes. Previous studies reported similar findings regarding seizures and brain injury on MRI.^{20,24} Seizures reflect brain dysfunction, which is, at least partly, irreversible. Cooling may postpone the emergence of seizures until rewarming.²⁴ The presence of seizures is not only associated with abnormal MRI findings but also with poor functional outcomes.

In a recent study on the usefulness of cerebral NIRS monitoring during TH, cerebral NIRS did not contribute to the prediction of short-term outcome.²⁵ This observation is in contrast with another study reporting higher $rcSO_2$ in infants with adverse outcomes following perinatal asphyxia and who had not undergone TH.¹ However, we found that $rcSO_2$ values were lower during the first 6 hours after birth. This may possibly be due to impaired autoregulation of cerebral blood flow following perinatal asphyxia.^{26,27} Another explanation may be that during the hours of cooling, sedative drugs together with TH itself may lead to a lower metabolic rate, a diminished oxygen demand and, as a consequence, this results in higher $rcSO_2$ values. In our study, the infants with adverse outcomes had higher $rcSO_2$ values at 72 hours after birth and after rewarming than infants with favorable outcomes. Wintermark et al pointed out that infants with severe HIE and adverse outcomes have a lower cerebral blood flow and extract less oxygen.²⁸ We speculate that due to neuronal loss in infants with severely adverse outcomes the metabolic rate remains low and, as a consequence, the $rcSO_2$ values remain high at 72 hours after birth, and after rewarming.

Shellhaas et al reported that the combination of systemic SO_2 and aEEG has predictive value at 6 hours before rewarming and during rewarming.²⁵ Cerebral NIRS did not contribute in prediction of their model, which suggests that systemic SO_2 is a better short-term prognostic value than $rcSO_2$.²⁹ We found that the combined predictive value of aEEG and NIRS at 48 and 72 hours after birth was higher than aEEG and NIRS alone. Our results are in accordance with other reports.^{1,12} Lemmers et al found an increase in the positive predictive value when cerebral NIRS and aEEG were combined at 12 hours postnatal age,¹² whereas Toet et al found a close correlation between cerebral NIRS and aEEG at

24 hours postnatal age.¹ Even though NIRS was previously not thought to contribute to the predictive value of aEEG, our study adds to the evidence that possibly the use of cerebral NIRS has the added clinical advantage of predicting outcome.^{12,13,27,30–33}

Our study has some limitations. We have a small sample size, similar as in other studies.^{12,13} This small sample size resulted in large CIs, and therefore the results of our study should be interpreted with some caution. We did not assess the effects of antiepileptic- or sedative drugs on the relationship between aEEG, NIRS, and outcome, because the small sample size limited the interpretation of statistical tests. Next, four infants died before rewarming. Their deaths were ascribed to irreversible circulatory failure or brain damage. This may have affected the predictive value of both aEEG and NIRS. Another limitation might be that aEEG is part of standard clinical care, and clinicians sometimes use aEEG in their decision to redirect care. However, a decision to cease intensive care treatment is never based solely on aEEG values. Rather, it is based on a combination of clinical state, a full EEG, and neuroimaging. NIRS was not a clinical parameter which was used to redirect care.

In conclusion, our study demonstrates that aEEG during TH has predictive value, although its predictive value is lower in comparison to the period before the introduction of TH as a treatment option for infants suffering from HIE. $rcSO_2$ has no predictive value in the initial phase of TH treatment. Nevertheless, from 48 hours onward its predictive value increases. After rewarming, $rcSO_2$ is an even better predictor of outcome than aEEG.

Conflict of Interest

None.

Acknowledgments

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