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Original Article

Correlation of amplitude electroencephalography in first 24 h after birth in perinatal asphyxiated neonates with short-term clinical outcome

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ABSTRACT

Objective: To correlate amplitude electroencephalography (aEEG) (in first 24 h after birth) in perinatal asphyxiated neonates with clinical outcome. **Materials and Methods:** This prospective cohort study was conducted in Jay Kay Lon Mother and Child Hospital, Government Medical College, Kota. All term asphyxiated neonates born with Apgar score of ≤7 at 5 min, admitted within 24 h of birth were included in this study. In each case, aEEG was recorded, and neurological examination was done at the time of admission and discharge. **Results:** Out of 72 cases, 39 neonates of hypoxic-ischemic encephalopathy (HIE) I had normal aEEG. Out of 24 neonates of HIE II, aEEG was normal in 7 and moderately abnormal in 17 neonates. All 9 neonates with HIE III had abnormal aEEG. Sensitivity of aEEG to identify seizures was 76.67%, specificity, positive predictive value (PPV), and negative predictive value (NPV) were 92.86%, 88.46%, and 84.78%, respectively. There were 41 neonates, who were neurologically normal at the time of discharge had normal aEEG. Out of 22 neonates, who were neurologically abnormal at discharge, aEEG was normal in 5 neonates and moderately abnormal in rest 17 neonates. Out of 9 neonates whose death occurred during treatment, aEEG was moderately abnormal in 2 neonates and severely abnormal in 7 neonates. Sensitivity of aEEG (normal pattern) for good outcome was 100% and specificity, PPV, and NPV were 83.87%, 89.13%, and 100%, respectively. Sensitivity of aEEG (abnormal pattern) for poor outcome was 83.87% and specificity, PPV, and NPV were 100%, 100%, and 89.13%, respectively. **Conclusion:** It is concluded that if aEEG is done within 24 h of birth in asphyxiated neonates, we can predict outcome of the baby. If early aEEG is normal then outcome tends to be favorable. On the other hand, if early aEEG is abnormal, then outcome tends to be unfavorable.

Key words: *Amplitude electroencephalography, Hypoxic-ischemic encephalopathy staging, Perinatal asphyxia*

Perinatal asphyxia and birth injuries together contribute to almost 29% of neonatal deaths [1]. The WHO has defined perinatal asphyxia as a "failure to initiate and sustain breathing at birth" [2]. The National Neonatal Perinatal Database, 2000 used a similar definition for perinatal asphyxia. Incidence of birth asphyxia was estimated as 4.6% of all births in community-based studies in India. Birth asphyxia is the cause of 20% of neonatal deaths in India [3]. In term infants with asphyxia renal, central nervous system, cardiac, and lung dysfunction occur in 50%, 28%, 25%, and 25% cases, respectively [4]. Apgar scores and measurements of fetal blood gases are widely used methods to determine outcome after birth asphyxia, but they are poor predictors of outcome of birth asphyxia [5-9]. Clinical assessment of the degree of hypoxic-ischemic encephalopathy (HIE) is a better predictor of outcome but may not become obvious until 12-36 h after birth [5,10,11]. Cranial tomographies, magnetic resonance spectroscopy are useful for prognosis but not until 24 h or more after birth [12,13]. Abnormal cerebral blood flow velocity measured with the Doppler technique has a high positive predictive value (PPV) when performed after 1-2 days of life but has not been evaluated during the first postnatal hours [14].

During the first few hours after birth, continuous amplitude-integrated electroencephalography (aEEG) recorded with a cerebral function monitor (CFM) is one of the most accurate bedside method to establish the neurologic prognosis in term asphyxiated infants [15,16]. Early detection of moderately or severely affected asphyxiated newborn (abnormal EEG) is essential to decide neuroprotective strategies such as head cooling, which should be started before 6 h of age. CFM or aEEG is a device for monitoring the background neurological activity. It uses a single, biparietal, or bitemporal leads (three wires) to obtain an EEG signal. This signal is filtered, semi-logarithmically compressed, and rectified. The output is displayed at a very slow chart speed 1 mm/min. As a result of this processing, the output is not a regular EEG signal but a representation of the overall electrocortical background activity of the brain.

This study was conducted to correlate early aEEG (1 channel) done within 24 h after birth with clinical outcome (HIE staging according to Sarnat and Sarnat) in perinatal asphyxiated neonates to mainly emphasize on the early prediction of outcome and also on the therapeutic aspects which may be of a particular benefit for asphyxiated newborns at high risk for developing hypoxic-ischemic encephalopathy.

MATERIALS AND METHODS

This prospective cohort study was conducted in the Department of Pediatrics, Jay Kay Lon Mother and Child Hospital, Government Medical College, Kota during the period of December 2014 to November 2015 after the approval of the Institutional Ethical Committee of Government Medical College. Sample size of 72 was calculated by following formula: $n = \frac{t^2 \times p(1-p)}{m^2}$ Where n=required sample size, t=confidence level at 95% (standard value of 1.96), p=prevalence of birth asphyxia, m=margin of error at 5%. Written consent was obtained from the parents or legal guardians.

All term (37-42 weeks) asphyxiated neonates (as per the WHO definition) born with Apgar score of ≤7 at 5 min, admitted within 24 h of birth in Department of Pediatrics were included in the study. Only those out born babies included in this study whose referral card had mentioned Apgar score. Neonates with major congenital malformation, chromosomal anomalies, or neonates under the influence of sedatives and antiepileptic drugs were excluded from the study.

Details were recorded for sociodemographic variables (age, sex), mode of delivery, and birth weight. After the stabilization and initial management, aEEG recording (CFM) was started. The aEEG was recorded by a single channel EEG from two central electrodes (C3 on left and C4 on right side) between 01 and 24 h of life. aEEG was recorded for minimum of 12-24 h. The filtered signal containing the main EEG frequencies is rectified and smoothened. Then, amplitude integrated before it is written out on slow speed paper (6 cm/h). Analysis of aEEG tracing done according to bandwidth limits [17]:

- Normal - Lower limit >5 μV and upper limit >10 μV
- Moderately abnormal - Lower limit <5 μV and upper limit >10 μV
- Severely abnormal - Lower limit <5 μV and upper limit <10 μV (Fig. 1).

Sarnat and Sarnat staging was done for each enrolled case. One channel (C3 and C4) aEEG tracing was correlated with clinical outcome (according to HIE staging) of the babies. The clinical outcome was concluded by neurological examination at the time of first examination (admission) and at discharge, in neonatal intensive care unit. In our study, we considered neonates who were successfully discharged and neurologically normal as good outcome, while those who were neurologically abnormal at discharge or dead, as poor outcome (Fig. 2).

Data obtained were analyzed using the Stata 13 (Texas, USA) software. Spearman correlation coefficient was used to find the significance of study parameters on categorical scale between two groups ($p<0.05$ was considered significant). Sensitivity, specificity, and predictive values of the tests were calculated.

RESULTS

There were total 12030 deliveries in our hospital, and total 110 newborns (inborn and outborn) were enrolled in our study. Out of 110 neonates, 72 cases included in this study based upon inclusion and exclusion criteria (Fig. 1) in which aEEG were done within 24 h of birth using CFM. Mean age at the time of aEEG recording was 10 h. In this study, 48 neonates (66.6%) were male and 24 (33.3%) were female. 58 (80.6%) were born by vaginal delivery and 14 (19.4%) neonates were born with cesarean section. Of these 72 neonates, 39 neonates were in HIE I, 24 neonates were in HIE II, and 9 neonates were in HIE III. Out of 58 neonates born by vaginal delivery, 29 were in HIE I, 21 were in HIE II, and 8 were in HIE III. In remaining 14 neonates (born by cesarean section), 10 were in HIE I and 3 were in HIE II and 1 was in HIE III (Table 1).

Seizures were present in 30 neonates (41.67%), and out of these 30 neonates, aEEG was abnormal in 23 (31.94%) neonates. Among the 42 neonates without seizures, aEEG was normal in 39 (54.16%) and it was abnormal in 03 (4.16%) neonates. Sensitivity of aEEG to identify correctly those who had seizures was 76.67% and specificity, PPV and negative predictive value (NPV) were 92.86%, 88.46%, and 84.78%, respectively. Table 2 summarizes aEEG changes in neonates with different HIE staging (statistically significant, spearman's coefficient=0.8617, p=0.0000). Table

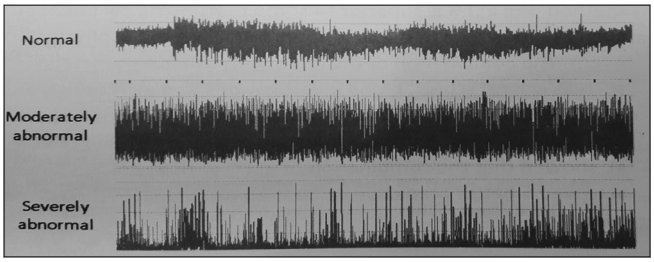

Figure 1: Analysis of amplitude electroencephalography tracings

Table 1: Baseline characteristics of the study

Characteristics	HIE I (%)	HIE II (%)	HIE III (%)
Total number of neonates	39 (54.16)	24 (33.33)	9 (12.5)
Mode of delivery			
Vaginal delivery	29 (50)	21 (36.20)	8 (13.79)
Cesarean section	10 (71.42)	3 (21.42)	1 (7.14)
Amniotic fluid			
Clear	29 (48.33)	22 (36.66)	9 (15)
Meconium stained	10 (83.33)	2 (16.66)	0
Birth weight			
<2.5 kg	20 (50)	13 (32.5)	7 (17.5)
2.5-3.0 kg	15 (55.55)	10 (37.03)	2 (7.40)
>3 kg	4 (80)	1 (20)	0

HIE: Hypoxic-ischemic encephalopathy

Table 2: Classification of aEEG according to severity of HIE

aEEG	HIE staging		
	HIE I (%)	HIE II (%)	HIE III (%)
Normal	39 (54.16)	7 (9.72)	0
Moderately abnormal	0	17 (23.61)	2 (2.77)
Severely abnormal	0	0	7 (9.72)

HIE: Hypoxic-ischemic encephalopathy, aEEG: Amplitude electroencephalography

Table 3: Relation of aEEG changes with clinical outcome

aEEG	Outcome		
	Successful (%)	Discharged with neurological abnormality (%)	Death (%)
Normal	41 (56.94)	5 (6.94)	0
Moderately abnormal	0	17 (23.61)	2 (2.77)
Severely abnormal	0	0	7 (9.72)

aEEG: Amplitude electroencephalography

3 provides relationship of clinical outcome with aEEG findings (statistically significant, spearman's coefficient=0.85, p=0.0000).

In current study, aEEG was normal in 46 neonates, of which good outcome was seen in 41 (89.13%) neonates and poor outcome was seen in 5 (10.87%) neonates. All 26 neonates with abnormal aEEG had poor outcome. Sensitivity of aEEG (normal pattern) for good outcome was 100% and specificity, PPV, and NPV were 83.87%, 89.13%, and 100%, respectively. Sensitivity of aEEG (abnormal pattern) for poor outcome was 83.87% and specificity, PPV and NPV were 100%, 100%, and 89.13%, respectively.

Table 4: Comparison of various studies for abnormal pattern in aEEG and poor outcome

Study	Number of neonates	aEEG timing	Sensitivity	Specificity	PPV	NPV
Present study	72	Within 24 hours	83.9	100	100	89.1
Thornberg and Ekström-Jodal [21]	38	Upon arrival in ICU	100	100	100	100
Hellström-Westas et al. [22]	82	First 6 h	94.7	89.3	85.7	96.1
Eken et al. [15]	31	Within 6 h	94.1	78.6	84.2	91.7
Toet et al. [16]	73	3 and 6 h old	87.5	73.3	77.8	84.6
Al Naqeeb et al. [17]	70	Median age 18 h	75	100	100	90.5
Shalak et al. [23]	50	Within 12 h	88.9	91.9	72.8	97.1
ter Horst et al. [24]	39	Median age 4 h 35 min	73.3	100	100	69.2
van Rooij et al. [25]	160	Within 6 h	95.2	85.3	87.8	94.1

PPV: Positive predictive value, NPV: Negative predictive value, aEEG: Amplitude electroencephalography, ICU: Intensive care unit

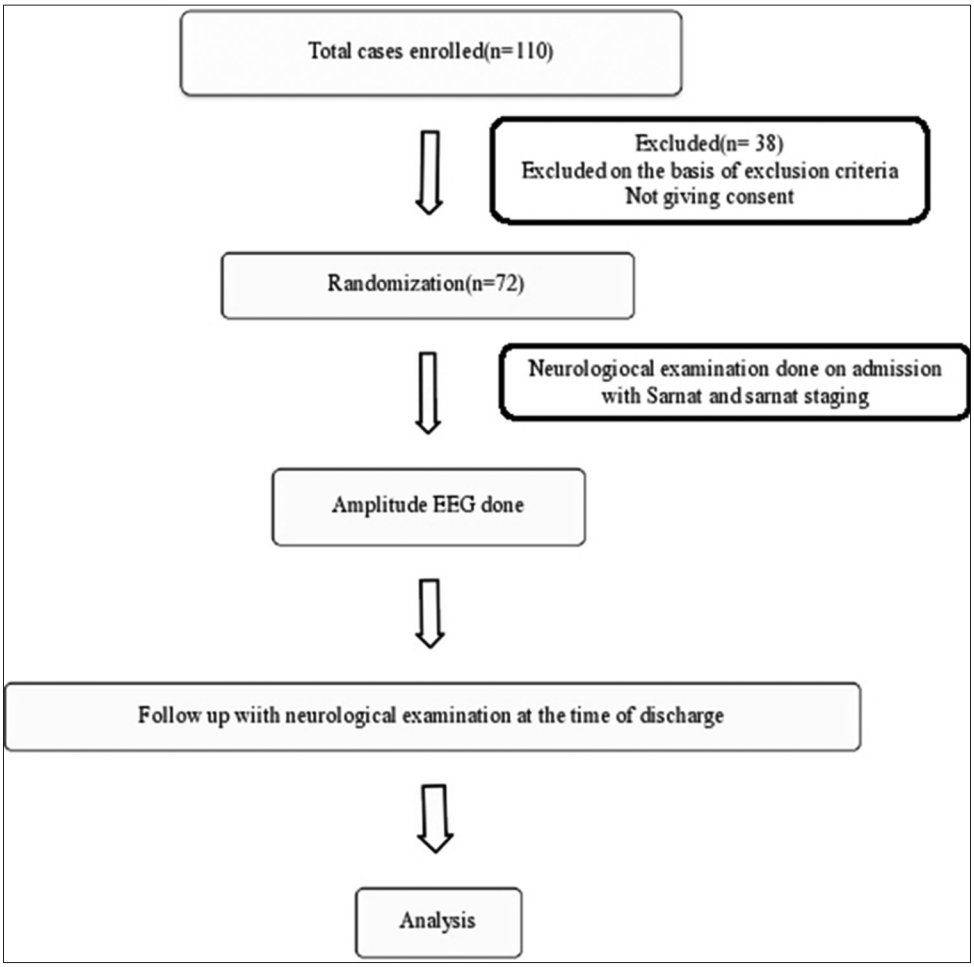

Figure 2: Study flow chart

DISCUSSION

Severe perinatal asphyxia may cause irreversible brain damage leading to death or serious neurological sequelae. The current study establishes that the aEEG pattern and its changes during the first 24 h after asphyxia provide fairly stringent prognostic information. In agreement with earlier studies of aEEG, the background activity seen in CFM contains the most important information [18,19]. We were able to show that aEEG has a good predictive value within 24 h of birth following perinatal asphyxia.

In current study, sensitivity of aEEG to identify correctly those who had seizures was 76.67%. Schettler reported sensitivity of aEEG for seizures was 78% through electrode position C3/C4 [20]. We were able to show that background pattern of aEEG in first 24 h has good correlation with clinical staging of HIE. aEEG was abnormal in all neonates with HIE III, while normal in all neonates with HIE I. However, in HIE II, aEEG was abnormal in 70.84% cases. Similar results were obtained in a previous study done by Toet et al. [16]. In current study, we observed a positive correlation of aEEG (abnormal pattern) (83.87% sensitivity and 100% specificity) with poor outcome. NPV of aEEG (abnormal pattern) for poor outcome was 89.13%, implying that if aEEG is not abnormal in first 24 h in a neonate with birth asphyxia, there is 89% probability that the neonate will be subsequently normal. Similar conclusions were also derived in previous studies (Table 4).

Possible reasons for the false negative results are only basal ganglia lesions or smaller one-sided brain damage. False positive readings may be seen due to the use of muscle relaxants. In our study, we did not get false positive results as muscle relaxants were not used in babies. Postnatal evaluation after perinatal asphyxia using aEEG can reliably predict neurodevelopmental outcome. Early aEEG might be useful for those neonates who require early intervention and treatment following perinatal asphyxia and also avoids unnecessary risks related to treatment in those neonates who do not require interventions. Limitation of our study was lack of long-term follow-up of these asphyxiated newborns in terms of outcome and neurological abnormality. Small sample size and exclusion of preterm asphyxiated neonates were other limitations.

CONCLUSION

It is concluded that if aEEG is done within 24 h of birth in asphyxiated neonates, we can determine the outcome of the baby. If early aEEG is normal then outcome tends to be favorable and accordingly, if early aEEG is abnormal then outcome tends to be unfavorable.

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