ORIGINAL ARTICLE

A Comparative Study of EEG and aEEG in Seizure Diagnosis in Infants Admitted to the NICU

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Abstract

Objectives

Seizure is a common sign in neonates hospitalized in the neonatal intensive care units (NICU) that may lead to morbidity and mortality. Most neonatal seizures are subclinical. Conventional EEG (cEEG) is the gold standard for detecting and monitoring seizures but is not widely available. Amplitude-integrated electroencephalography (aEEG) has been used for over a decade to evaluate infants with seizures. In this study, we tried to determine the efficacy of aEEG as a widely available diagnostic tool in diagnosing seizures.

Materials & Methods

All cases with seizures or suspicious seizures were admitted to the NICU of the Children's Medical Center for one year. cEEG and aEEG were performed for these infants. aEEG was recorded for at least six hours with a description of the tracing. Clinical information, outcomes, and questionnaires (patient information) were recorded in detail. The obtained data were analyzed with the SPSS version 24 software.

Results

Eleven out of twenty-five aEEG recordings were abnormal; other patients showed normal aEEGs. The most common clinical and neurological manifestations were seizure (68%) and hypotonia (28%); the mortality rate was 12%. No significant correlation was observed between aEEG findings and gender, age, familial relation, outcome, ultrasound result, type of seizure, and underlying disease.

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Conclusion

Studies showed variable sensitivity and specificity values for aEEG. aEEG cannot be recommended as the only way to diagnose and manage seizures in neonates. However, Good accessibility and ease of working with aEEG promote a tendency to use this procedure as a screening tool.

Keywords: aEEG, seizures, neonates.
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Introduction

Neonatal seizures are newborns' most common neurological manifestation and often the first sign of neurological dysfunction. (1-5). Seizures occur more frequently in the neonatal period than at any other time, particularly in the first one or two days to the first week from birth (6, 7). The incidence of neonatal seizures varies by weight and gestational age. In NICUs, the incidence is as high as 8-15% (1, 8- 11). It seems that seizures could affect the maturation and development of the brain in a critical period and are associated with a significant incidence of brain injury and long-term neurodevelopmental delay (7, 12-14). They often signify serious malfunction or damage to the immature brain and constitute a neurological emergency demanding urgent diagnosis and management (15-17).

Neonatal seizures can be challenging to diagnose, as seizure activity in newborns is often not clinically apparent. About 80% of seizures are occult; hence, clinical observation alone could hamper the successful diagnosis of neonatal seizures (18-19). On the other hand, seizures may be overdiagnosed because clinical paroxysmal movements do not correlate with EEG seizure activity. Using only EEG to determine neonatal seizures causes misdiagnoses of subcortical seizures. Therefore, a combination of clinical and EEG findings helps diagnose seizures in neonates (20- 22).

Conventional electroencephalography (cEEG) is a critical investigation and gold standard for identifying epileptiform events accurately. (23-26). cEEG's availability is limited due to the complexity of the equipment and the need for specialized staff to apply the numerous electrodes, making it difficult to use in most centers in many countries. Furthermore, its results are unavailable online to help clinicians manage patients (6, 27-30). aEEG is a simple method to gather EEG information (amplified, filtered, and compressed) using fewer electrodes, which could detect seizures and provide real-time information on brain electrical activity. Today, aEEG is used routinely in an increasing number of NICUs as a quantitative predictor and provides a global overview of brain cerebral activity(27, 31-35).

aEEG can be a good screening tool for diagnosing seizures in infants. Although it is less sensitive and specific than cEEG, which is the gold standard and

is not to be replaced, its sensitivity and specificity are acceptable for a screening method. However, aEEG is acceptable in predicting outcomes when the background is mildly or severely abnormal.

Materials & Methods

The present study was conducted for one year (April 1st, 2018, to May 30th, 2019) by a neonatologist on twenty-five neonates with suspicious seizures who were admitted to the NICU of the Children's Medical Center, Tehran, Iran, affiliated with the Tehran University of Medical Sciences.

The local ethics committee approved the study proposal, and informed consent was obtained from the neonates' parents. Obtaining parental consent was part of the in-department protocol. Neonates who met the inclusion criteria.

Inclusion criteria included neonates with clinical criteria:

- Seizure (tonic, clonic, subtle, and combined)
- Hypertonia
- Hypotonia
- Apnea without any sources
- Decreased consciousness

Exclusion criteria included neonates with asphyxia diagnosis, death before aEEG acquisition, and parent dissatisfaction.

The study's limitations included lack of accuracy of some seizures in neonates, device failure and program disruptions, interference of EEG waves and some drugs (midazolam), parental dissatisfaction, the small number of patients, and short study time.

The EEG diagnostic method was performed based on the international 10/20 system. Moreover, the aEEG evaluations were done by installing four electrodes on the infant's head (on c3, c4, p3, p4) by a trained nurse and recording for at least six hours with a description of the whole tracing. Patients' diagnoses and relevant clinical information were also recorded. The obtained aEEG recordings were collected and interpreted by both fellows of neonatology and pediatric neurologist subspecialist clinicians carefully and separately.

Findings were recorded using questionnaires, including patient information: disease symptoms, gender, age, and duration of hospitalization.

The length of hospitalization determined the outcome, the response to treatment, and discharge from NICU or death.

Statistical analyses

Descriptive analyses of the data were performed using the McNemar test. Pearson's chi-squared test. The analyses were performed using SPSS software version 24, and a p-value of less than 0.05 was considered statistically significant.

Results

Twenty-five patients in the NICU department were enrolled in the present study. Of the neonates, 13 (52%) were males and 12 (48%) were females. The mean age of neonates was 16/08 (±13/3) days. Also, the mean gestational age was thirty-eight weeks (±2/01).

The most common neurological manifestations were tonic, colonic, subtle, and mixed seizures (68%) and hypotonia (28%), and the mortality rate was 12%.

In this study, twenty-five patients were examined using EEG and aEEG methods. The pediatric neurologist interpreted the EEGs. Of the twenty-five patients studied, eight (32%) had normal EEGs, and 17 (68%) had abnormal EEGs.

Fourteen newborns (56%) had normal aEEGs, and 11 (44%) had abnormal aEEGs. Table 1 shows

different aEEG results seen in affected neonates.

The results show no significant correlation between aEEG findings (normal and abnormal) and age, familial relation, outcome, ultrasound result, type of seizure, and underlying diseases. No relation was observed between age, familial relation, outcome, ultrasound result, type of seizure, and underlying disease and EEG findings.

This study also investigated the relationship between aEEG and EEG in neonates with seizures. However, Table 1 shows a significant statistical relationship between EEG and aEEG findings in newborns with seizures ($p< 0.004$).

Finally, the measure of agreement between pediatric neurologists and fellows of neonatology reports based on aEEG findings was 0.724 (strong) and statistically significant (p-value = 0.003) (Table 4).

Discussion

This study reported EEG and aEEG in neonates with suspicious seizures and obtained the six-hour aEEG tracings of twenty-five patients with different types of seizures for one year. Among twenty-five neonates, 68% had abnormal EEG, and 44% showed abnormal aEEG. In Ms. Theda's study, 70% had abnormal aEEG (36). The findings of aEEG were abnormal in seven boys and four girls and normal in five boys and eight girls. Thus, no significant correlation was observed between the findings of aEEG (normal and abnormal) and gender.

In this study, the most frequent clinical symptoms were seizures (68%) and other neurologic signs (hypotonia, apnea, and cyanosis) (32%). The present study's results are consistent with the results reported by Kadivar et al., who showed that aEEG is not 'diagnostic' in IEM (Inborn error of metabolism) (27).

In this study, neonatal seizures were tonic (most common type), clonic, subtle, and mixed. In other studies, asphyxiated infants were examined. This study examined the difference between the types of seizures and aEEGs. The results showed no significant relation between aEEG findings and the type of seizures. Thus, it seems that aEEG abnormalities help monitor neonates' brain function. In this study, EEG results were consistent with aEEG results (p-value < 0.004).

As reported, no relation was observed between age, familial relation of the parents, the outcome, ultrasound results, type of seizure, underlying disease, and aEEG and EEG findings.

Comparing the aEEG method and standard EEG method, the aEEG method had 64% sensitivity and 57% Specificity. However, in Osredkar's study, aEEG sensitivity was 50%, and its specificity was 100% (37). In Spitzmiller's aEEG analysis, the sensitivity of aEEG was 91%, and the specificity was 100%. (35). Other studies also reported that aEEG has high sensitivity and specificity in predicting neurodevelopmental outcomes for screening asphyxiated full-term infants (26-29).

We have also found a significant agreement between pediatric neurologists and neonatologists on the aEEG report. The agreement rate was 84% between pediatric neurologists and neonatologists in reading and reporting aEEG, which is consistent with the results reported by Kadivar et al. (27)

Regarding the small number of patients in one health center in this study, more studies with larger populations are needed to determine the efficacy of aEEG in diagnosing neonates with seizures. However, aEEG is a new technology in this center, and this study was conducted for the first time and showed the capability and effect of training in neonatologists.

In conclusion

Due to the simplicity of using aEEG by the educated NICU staff, this device could be an excellent hands-on procedure for screening seizure problems in the NICUs. However, further well-developed studies with larger populations are needed to compare EEG and aEEG in neonates admitted with seizures to the NICU.

Abbreviations

aEEG: Amplitude - integrated electroencephalography; CNV: Continuous normal voltage; DNV: Discontinuous normal voltage; BS: Burst suppression; EEG: Electroencephalography; IEM: Inborn error of metabolism; NICU: Neonatal Intensive Care Unit.

Acknowledgment

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Availability of data and materials

The datasets of the current study are available from the corresponding author upon reasonable request.

Authors' Contribution

Maliheh Kadivar, MD, presented the main idea of this research project and supervised the implementation of the project and data collection along with the analysis. Elaheh Movahedi Moghadam collaborated with Maliheh Kadivar in data collection, study implementation, and manuscript preparation. The study was part of Yalda Taghipour's thesis for a subspecialty in neonatology dissertation, and she collected data and filled out the forms. Razieh Sangsari, MD, contributed to the study design. Maryam Saeedi, MD, collaborated as the scientific counselor of the project and data analysis. Reza Shervin Badv, MD, interpreted the aEEG and EEG reports. Mahmoud Reza Ashrafi, MD, reviewed the data collection of the study.

Ethics approval and consent to participate The local ethics committee of the Neonatal Health Research Center, Research Institute for Children's Health, Shahid Beheshti University of Medical Sciences, Tehran, Iran, approved the study (99/p/146- 99/6/21). The parents of all patients provided informed written consent, which the ethics committee approved.

Conflict of Interest

The authors declare that they have no competing interests.

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