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ORIGINAL ARTICLE

Description of the First Newborns Monitored Using Amplitude-Integrated Electroencephalogram in a Private Maternity Hospital in Northeast Brazil.

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Electroencephalography, Infant, Seizures.

Abstract

Continuous brain monitoring using amplitude-integrated electroencephalography (aEEG) enables the detection of subclinical seizures and their early treatment, promoting neuroprotection and preventing permanent neurological injuries. The objective of this study was to analyze the profile of newborns (NB) monitored remotely by a team using this methodology in a private maternity hospital in the northeastern region of Brazil. **Methods:** This was an observational, descriptive, and cross-sectional clinical study. A convenience sample was used, including all sequential newborns submitted to neuromonitoring from February 2021 to June 2022. Maternal and clinical data of the NB were collected through a form designed by the researchers and subsequently subjected to descriptive statistical analysis using R Core Team 2022 software (Version 4.2.2). The study was submitted and approved by the Ethics Committee under CAAE 55437521.8.0000.5371. **Results:** A total of 16 NB were included. The most common indications for aEEG monitoring were suspected seizures (37.5%) and the presence of witnessed clinical seizures (18.75%). During the study, 5 NB (31.25%) could have their anticonvulsant medication discontinued early after aEEG monitoring; 5 NB (31.5%) with suspected clinical seizures had the hypothesis ruled out and did not start anticonvulsant therapy, and in 18.8% (n=3) of patients, subclinical seizures were observed in the examination, leading to the initiation of treatment. **Conclusion:** aEEG allowed the medical team to suspend or avoid the unnecessary use of anticonvulsants in 81.2% of the investigated NB and safely maintain or initiate anticonvulsant therapy in 18.8% of cases.

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INTRODUCTION

The neonatal period is the period with the highest incidence of seizures throughout life.[1] The incidence of seizures in the neonatal period ranges from 1 to 3.5 for every 1,000 live births.[2]

The most common etiologies for seizures in this phase are: hypoxic-ischemic encephalopathy, ischemic stroke, intracranial hemorrhage, brain malformation, inborn errors of metabolism, infections, and others of lower incidence.[3] It is important to highlight that 80% of epileptic seizures are completely subclinical within a neonatal intensive care unit.[4,5] Another difficulty faced is the wide variety of paroxysmal non-epileptic movements in this age group, which are difficult to differentiate from clinical seizures and may lead to unnecessary treatments.[6,7] With the advancement of technology, a simplification of conventional continuous electroencephalography (EEG) performed using a smaller number of channels was developed with the aim of simplifying brain neuromonitoring, and is called amplitude-integrated electroencephalography (aEEG). This is also a non-invasive modality, performed at the bedside and in real time, with a good correlation with EEG.[8–11]

aEEG is usually recorded from one or two channels derived from parietal, central or frontal leads, and is very useful for identifying seizures in newborns. Current monitors display, in addition to the compressed tracing, the corresponding conventional EEG (aEEG/EEG), which increases the likelihood of detecting brief and single seizures. It is also associated with video monitoring, enabling the examiner who issues the report remotely to correlate the tracing with the patient's clinical condition, reducing errors in interpretation and enabling the exchange of information between teams.[12–14]

Newborns at high risk of seizures or permanent brain damage require continuous monitoring to detect seizures and prognosis of neurological injuries in newborns who have suffered neonatal hypoxia. The main advantages of aEEG over EEG are fewer electrodes on the scalp, which can be applied by the neonatal team and maintained for long periods for continuous monitoring; the on-screen display is easier to interpret, even by properly trained neonatal bedside staff; and less time is required to review the tracing due to the time-compressed nature of aEEG. Due to these advantages, aEEG is gaining popularity in neonatal intensive care units (NICUs) worldwide and is used by the neonatal team to assist in patient management.[14]

Our objective was to analyze the epidemiological profile and clinical outcome of the first newborns monitored using aEEG in a private maternity hospital in the northeast region. The use of remote monitoring was tested with the pioneering use of the equipment in the northeast region, where we sought to understand the feasibility and real benefits of the technology for the monitored newborns.

METHODS

This is an observational, analytical, descriptive, and cross-sectional clinical study. A convenience, non-probabilistic sample was used, which included all sequential newborns who underwent neuromonitoring from February 2021 to June 2022. The neuromonitoring technology used was amplitude-integrated electroencephalography associated with raw EEG reading (aEEG/EEG) using 3 channels (C3-P3; C4-P4; P3-P4). Newborns who could not complete at least 12 hours of monitoring and those who could not complete the data collection spreadsheet were excluded. Using a form prepared by the researchers, data regarding maternal comorbidities and complications, newborn epidemiological data, birth conditions, clinical evolution, treatments performed, and outcomes were collected and plotted in a Microsoft Excel® spreadsheet. Descriptive statistical analysis was performed using R Core Team 2022 software (version 4.2.2). For quantitative variables, measures of central tendency (mean and median), measures of dispersion (standard deviation - SD), and measures of position (interquartile range - IQR) were presented, for categorical variables, relative and absolute frequencies.

The study was submitted to and approved by the Ethics Committee under number CAAE 55437521.8.0000.5371.

RESULTS

Sixteen patients who received neuromonitoring during the period were included.

The average age of the pregnant women was 31.7 (± 5.4 years), and the majority (75%) had at least 6 prenatal consultations. Most mothers did not have any comorbidities before pregnancy (87.7% n=14). The only previous diagnoses were (n=2): uterine prolapse (with pessary use) and type 2 diabetes mellitus. Approximately 56.6% of pregnant women presented complications (n=9), of which: 33.3% presented hypertensive disease specific to pregnancy (n=3), followed by other patients with overlapping or non-overlapping alterations, such as alteration in the amount of amniotic fluid, whether polyhydramnios or oligohydramnios (n=2), previous fetal or neonatal death (n=2), urinary tract infection (n=2), premature placental abruption (n=2) and also premature rupture of membranes (n=1), gestational diabetes mellitus (n=1) and fetal malformation (n=1). Most deliveries were by cesarean section (81.3% / n=13). Regarding the demographic data related to the newborns, the average weight of the newborns was 2,343.1 g and the median was 2,915 g, while the average gestational age was 34.1 weeks, and the median was 37 weeks. The vast majority (81.3%) of the newborns were classified as appropriate for gestational age (AGA), with 12.5% being SGA and 6.3% LGA.

Among the newborns in the sample, 62.5% (n=10) presented some complication in the peripartum period. Non-cephalic presentation occurred in 4 (25%) of the newborns and 18.8% of them were from premature birth (n=3) and

12.5% presented meconium-stained amniotic fluid (n=2). Other complications with only one patient each were: fetal bradycardia, use of forceps or vacuum extraction and rupture of membranes >18 hours.

Most newborns (87.7%) required some type of resuscitation maneuver in the delivery room (n=14). The most used maneuver (62.5%) was positive pressure ventilation with a bag-valve mask (n=10). Other maneuvers also used were, in order of frequency: upper airway aspiration (50%; n=8), orotracheal intubation (43.4%; n=7), cardiac massage (18.8%; n=3), use of adrenaline (12.5%; n=2) and in only one case was expansion performed with 0.9% saline solution. Most newborns (93.8%) had an Apgar score >= 6 in the fifth minute (n=15).

The diagnosis for admission to the NICU was mainly (26.30%) due to episodes of cyanosis to be clarified (n=5), where the differential diagnosis with convulsive crises was necessary or was already highly suspected (with use of anticonvulsant with clinical treatment in one of them). In second place (21%), suspected neonatal asphyxia (n=4). In addition, other more common diagnoses, whether overlapping or not as causes of hospitalization, were extreme prematurity (21%; n=4) and isolated diagnoses in only one patient each: neonatal sepsis, extremely low weight, congenital hydrocephalus and convulsions. During the hospitalization period, 14 patients (87.5%) presented some complication, the most common being sepsis (56.6%) in 9 patients. In addition, 2 patients (12.5%) presented pulmonary hemorrhage, and 2 patients (12.5%) presented clinical convulsions. Other less common complications described in only one patient each: coagulation disorder, renal failure, urinary tract infection, pulmonary hypertension, and one patient had mild left ventricular dysfunction.

The blood gas analysis collected in the first hour of life in 9 patients (56.3%) showed a mean pH of 7.2 (± 0.1) and a median of 7.1. Regarding base excess, performed in 8 patients in the first hour of life (50%), the mean was -9.2 (± 6.6) and the median -7.5.

The indications for neuromonitoring are presented in Table 1 below, with the majority (56.2%) being indicated for suspected or already treated seizures (n = 9).

Table 1. Indication of the 16 patients for neuromonitoring from February 2021 to June 2022.

Neuromonitoring indication	n = 16	% (100%)
	6	37.50%
Clinical seizure spell in treatment	3	18.75%
Perinatal asphyxia/Hypoxic-ischemic encephalopathy	2	12.50%
Extreme prematurity	2	12.50%
Hemodynamic instability	1	6.25%
Severe brain malformations	1	6.25%
Undiagnosed cyanosis	1	6.25%

Legend: n – absolute frequency. % – relative percentage frequency.
Source: Authors, 2023.

Most patients (62.5%) were using sedative medications at the time of neuromonitoring (n=10). Dexmedetomidine was the most used (56.6%, n=9), followed by midazolam (12.5%, n=2) and fentanyl in one patient. Vasoactive medications were used by 9 (56.3%) patients, with 8 (50%) using dobutamine, 6 (37.5%) using adrenaline and 3 (18.8%) using dopamine.

In total, 13 newborns (81.3%) used neuromonitoring during the 24-hour period. Only 1 newborn for 12h, 1 newborn for 48h and 1 newborn for 72h, with 13 newborns (81.3%) using the time recommended in the protocol, according to the indication. Only 2 (12.5%) patients performed 24h less than suggested and 1 patient performed 36h less. 3 newborns (18.8%) presented epileptic seizures treated and controlled during the monitoring period.

Among the patients, 13 (81.2%) paid for the exam privately and 3 (18.8%) through a health insurance plan. The results of the monitoring reports are presented in Table 2.

Regarding the outcome of hospitalization, discharge from the ICU/Hospital was the most prevalent (75%; n=12). Other outcomes were death (18.75%; n=3) and discharge from the ICU/Transfer (6.25%; n=1).

Regarding the use of anticonvulsants (ACV), the table below shows the reports and the conduct adopted after the aEEG was performed separately. (Table 3).

DISCUSSION

The study showed that the aEEG exam was important to provide the necessary assertion for the medical team to suspend anticonvulsants previously initiated in the face of a prior unfounded clinical suspicion in most cases. In addition to this great benefit, it also enabled starting or maintaining the medication in the face of confirmation of suspected seizures.

The sample of pregnant women was characterized by an average age over 30 years, confirming a national trend, and gestational age alone did not prove to be a risk factor for neonatal hypoxia. It is well demonstrated that diseases such as preeclampsia and eclampsia can increase the risk of neonatal asphyxia by up to 10 times. Since this was a private maternity hospital, most pregnant women followed the routine of prenatal consultations and did not have comorbidities. The predominance of cesarean deliveries reflects a trend in the maternity hospital where the study was conducted, as it is a private hospital with a high rate of elective cesarean deliveries. In fact, most of the newborns were classified as full-term, appropriate for gestational age, and with adequate birth weight. It is important to realize that neonatal hypoxia can occur even in this population of pregnant women without major risk factors, which reinforces the need to maintain a trained team in maternity hospitals and birth centers, since complications in the peripartum period cannot be ignored, as they can negatively affect the outcome of the newborn, requiring equally cautious care.[15,16]

Table 2. aEEG reports of the 16 patients from February 2021 to June 2022, after neuromonitoring.

Outcome	n = 16	% (100%)	aEEG report
Suspected seizure ruled out, without use of anticonvulsant	5	31.25%	No ES
Suspected seizure ruled out, anticonvulsant discontinued	5	31.25%	No ES
Suspicion ruled out without prior clinical symptoms	2	12.5%	No ES
Seizure confirmed and continued use of anticonvulsant	1	6.25%	With ES
Seizure confirmed, subclinical aEEG and continued use of anticonvulsant	1	6.25%	With ES
Started using anticonvulsants after confirmation of subclinical seizures	1	6.25%	With ES
Neonatologist maintained anticonvulsant therapy even with a normal aEEG report during the period performed, due to clinical indication	1	6.25%	With ES

Legend: n – absolute frequency. % – relative percentage frequency. ES – Epileptic seizure.
Source: The author, 2023.

Table 3. Use of ACV in the 16 patients from February 2021 to June 2022, after the aEEG was performed.

Approach	n = 16	% (100%)	aEEG report
Did not start the ACV	7	43.70%	No ES
Discontinued the ACV	5	37.50%	No ES
Maintained the ACV	3	18.75%	With ES
Started the ACV	1	6.25%	With ES

Legenda: n – absolute frequency. % – relative percentage frequency. CE – Epileptic seizure.
Source: Authors, 2023.

The stressful events that culminated in hypoxia occurred during intrapartum or in the immediate postpartum period, where most of the monitored newborns required prior resuscitation in the delivery room and continued care in the NICU environment, reinforcing the unpredictability of the situation. This profile reinforces the importance of an adequate assessment of all newborns at birth, providing immediate assistance and clinically assessing neurological development (using the Sarnat scale), as well as collecting blood gas analysis early in cases that required resuscitation to indicate appropriate brain monitoring. Among the clinical neurological signs that alert physicians to the possibility of brain damage, seizures are the most frequently observed neurological sign in the NICU. In this regard, pediatricians and neonatologists face a major challenge: detecting seizures through clinical examination alone. The major difficulty here is differentiating benign movements, tremors that can affect both newborns without diseases and those with neurological problems. For example, benign sleep myoclonus, which can occur from birth to 6 weeks of age. Therefore, non-epileptic paroxysmal manifestations can occur in newborns, and it is important to identify them through clinical foundations and, eventually, with the help of aEEG, since newborns with poorly managed seizures have a 10% increase in mortality and up to 50% in neurological morbidity.[17-20] Regarding their diagnosis, it is important to confirm with electroencephalography through continuous monitoring, which is the only way to detect neonatal seizures, especially in premature newborns, as they have a spectrum of uncoordinated movements and a subtle semiology, so that in most cases, seizures in newborns are only electrographic or subclinical.

For this reason, screening for seizures through exams is already a reality and it is recommended by the American Clinical Neurophysiology Society for Neonates.[21] Therefore, the clinical diagnosis of neonatal seizures can be extremely flawed, requiring a form of monitoring that can identify subclinical seizures, such as aEEG, because it has continuous monitoring, it is readily available, less invasive, easy to set up and allows prolonged recordings.[22] aEEG has a sensitivity of 85% and 90% specificity when interpreted by experienced people, as is the case in the present study, through a team of neurologists on standby, trained in the method.[23] There are several diseases in the neonatal period associated with a high risk of developing sequelae and that should be indications for neuromonitoring with continuous aEEG. One example is perinatal asphyxia, which represents the third most common cause of neonatal death after premature birth. Severe infections, severe or moderate encephalopathy, and prematurity, which has a high risk of survival accompanied by neurological deficits.[24–28] Based on all this information, aEEG is an appropriate screening tool for detecting newborns who require conventional electroencephalography in the NICU, especially if the two techniques are combined. With appropriate use of aEEG, neonatal seizures, which are associated with adverse long-term cognitive and neuromotor outcomes, can be prevented and identified early. Considering the severity of hypoxic-ischemic injury, worsening neurodevelopmental outcome with increasing seizure severity may harm the developing human brain, especially in preterm infants.[29–31]

On the one hand, failing to treat these seizures properly can lead to long-term neurological sequelae

and damage. On the other hand, and no less important, unnecessarily treating the newborn's benign movements with anticonvulsants can lead to damage caused using the medication, since most cases lead to neurological, renal, hepatic and bone marrow cell damage. In the public service, where tests such as electroencephalography and neurologists are difficult to access, this leads to prolonged use of these medications for long periods, generally over two years. Anticonvulsants cause damage, as observed in a previous study. Carbamazepine was the most prescribed antiepileptic medication for children and its side effects are water retention, sedation, hypersensitivity reactions, ataxia, leukopenia, blurred vision and, most rarely, liver failure. Valproate also poses risks due to its undesirable effects of weight gain, nausea, hair loss and fetal malformations. Both medications, as well as phenytoin, pose risks for brain malformation, and can cause brain degeneration. For this reason, their use must be very precisely indicated in order to avoid unwanted side effects, especially if their use is poorly indicated.[32–34] Phenobarbital, which is the drug most commonly used in the neonatal period, leads to impairment of the central nervous and respiratory systems, apoptosis of brain cells, cholestasis and increases the risk of neurological diseases in the long term.[35] For this reason, their use must be very precisely indicated in order to avoid unwanted side effects, especially if their use is poorly indicated and there was a great benefit in early withdrawal of these drugs. This study showed that the physician's conduct could be guided by neuromonitoring, and in most cases, antiepileptic medication was suspended or not started, avoiding side effects that these drugs can cause.

Recent studies show that EEG before discharge enables early withdrawal of anticonvulsants to reduce long-term side effects in infants.[36]

The initiative under study enabled monitoring by a remote team, so that a maternity hospital in the Northeast could benefit from current technology.[37]

We mention some limitations of the study, as it was carried out in a single health unit and with a still small number of patients. As it is still in the contracting phase with health insurance companies, in most cases it depends on private funding, making it difficult to carry out in all indicated cases. Despite the difficulties, it shows the potential of technology to assist the physician in decision-making within the NICU for the benefit of newborn care.

CONCLUSION:

Performing amplitude-integrated electroencephalography enabled the medical team to make important decisions in all patients evaluated, sometimes enabling the discontinuation or avoidance of unnecessary use of anticonvulsants (81.2% of cases) or enabling the maintenance or safe start of anticonvulsants in the remainder of the sample (18.8% of cases).

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