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Original contribution

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Neonatal Seizures: etiology, electroencephalographic patterns, and outcome

Convulsiones neonatales: etiología, patrones electroencefalográficos y evolución.

Abstract

Introduction: Neonatal seizures (NS) constitute the clinical expression par excellence of a dysfunction in the Central Nervous System and present a high incidence.

Objective: To review etiology, electroencephalographic patterns, and the outcome of neonatal seizures, as well as to seek associations between NS and other neurological risk factors.

Methods: We studied 22 patients with NS. Pre-, peri-, and postnatal antecedents were collected. Electroencephalogram (EEG) was performed, classifying the results into normal, mild, moderate and severe alterations. A general linear model was used to demonstrate possible associations between seizures and other neurological risk factors.

Results: Hypoxic-ischemic encephalopathy was the most frequent etiology, approximately 40% of the subjects showed a good outcome, and the most frequent sequel was epilepsy (40.9%). EEG was normal only in 13.63% of patients. The analysis of possible statistical associations showed statistically significant associations between the EEG outcome and the patient's outcome ($p=0.015$), between gestational age and outcome ($p=0.003$) as well as between birth weight and outcome ($p=0.003$).

Conclusions: The prediction of morbid damage has made it necessary to search for biochemical, neurophysiological, and neuroimaging indicators in order to identify early lesions that threaten the satisfactory evolution of children due to morphological and functional alterations.

Keywords

neonatal seizures, etiology, electroencephalographic patterns, and evolution.

Resumen

Introducción: Las convulsiones neonatales (CN) constituyen la expresión clínica por excelencia de una disfunción en el Sistema Nervioso Central y presentan una elevada incidencia.

Objetivo: Revisar la etiología, los patrones electroencefalográficos y la evolución de las convulsiones neonatales, así mismo se intentará buscar asociaciones entre las CN y otros factores de riesgo neurológico.

Métodos: Se estudiaron 22 pacientes con CN. Se recogieron antecedentes pre, peri y post natales. Se realizó estudio electroencefalograma (EEG), clasificando los resultados en normal, alteraciones ligeras, moderadas y graves. Se utilizó un modelo lineal general para demostrar las posibles asociaciones entre las convulsiones y otros factores de riesgo neurológico.

Resultados: La encefalopatía hipóxico isquémica fue la etiología más frecuente, aproximadamente el 40% de los sujetos mostraron una buena evolución y la secuela más frecuentes fue la epilepsia (40.9%). El EEG fue normal sólo en el 13.63% de los pacientes. The analysis of the possible statistical associations showed statistically significant associations between the EEG result and the outcome of the patient ($p=0.015$), between gestational age and outcome ($p=0.003$), and between birth weight and outcome ($p=0.003$).

Conclusiones: La predicción de daños mórbidos ha hecho necesaria la búsqueda de indicadores bioquímicos, neurofisiológicos y de neuroimágenes con la finalidad de identificar tempranamente lesiones que amenacen la evolución satisfactoria de los niños, por alteraciones morfológicas y funcionales.

Palabras clave

convulsiones neonatales, etiología, patrones electroencefalográficos, evolución.

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Introduction

Seizures in the neonatal period (NS) constitute the characteristic clinical expression of a dysfunction of the Central Nervous System (CNS).¹ The incidence of NS is 0.15-1.4% of newborns.²

It is not always easy to recognize them and they can go unnoticed, especially in the preterm newborn—this is related to the anatomical, biochemical, and physiological development of the CNS during the perinatal period.¹ The clinical and electroencephalographic manifestations differ from those of a newborn with greater neurological maturity, reflecting functional differences due to a lower degree of myelination.³

The occurrence of seizures in the newborn is of great importance because of its association with high rates of neurological morbidity and mortality; furthermore, they require urgent diagnosis and treatment to prevent the aggravation of underlying brain lesions.^{4,5}

The electroencephalogram is not only one of the few methods that allow a functional study of the CNS, but it also has the advantages of being safe and of low economic cost in comparison with the neuroimaging techniques—such as tomography and magnetic resonance imaging—which are structural methods that allow us to visualize the lesion but do not inform us about the pathophysiological process.

The aim of this study is to review the etiology, the electroencephalographic patterns, and the outcome of seizures in the prenatal period, as well as to establish possible associations between NS and other neurological risk factors.

Methods

Twenty-two newborns admitted to the Neonatal Care Unit of the Juan Manuel Márquez Pediatric Teaching Hospital with the diagnosis of neonatal seizures were studied. We collected pre-, peri-, and postnatal antecedents, gestational age, and birth weight. The patients attended neurodevelopment consultations for periodic evaluations for at least 12 months.

Electroencephalographic evaluation

The electroencephalographic record was obtained in spontaneous sleep with an approximate duration of 60 minutes. For the monitoring of other polygraphic variables (electrooculogram, electromyogram, and oxygen saturation) we used the digital electroencephalographic system MEDICID-5 (Neuronic SA) with amplifiers with a gain of 10,000, sampling frequency of 200 Hz, and filters with a 0.5-30 Hz bandwidth. We used 19 surface electrodes placed according to the international 10-20 system. Shorted electrodes located on both earlobes were used as reference. The visual inspection of the EEG was done offline by two experts independently.

The electroencephalographic studies were classified as normal, with minimal alterations (immaturity of base rhythms, interhemispheric asynchrony, decreased voltage), moderate alterations (persistent focal or generalized acute spikes and waves), critical tracing (with patterns of focal disturbances during crises, focal or multifocal monorhythmic discharges during crises), and severe alterations (presence of isoelectric tracing or with a burst-suppression pattern).⁶

Death or manifestations of serious sequelae (epilepsy, psychomotor development retardation, infantile cerebral palsy) were considered “unfavorable outcome.”

Statistical Analysis

We calculated the mean and the standard

deviation as well as the distribution of risk factor frequencies. A general linear model was applied for the statistical analysis of the data, accepting $p < 0.05$ as statistically significant.

Ethical Considerations

The research was approved by the Research Ethics Committee of the Juan Manuel Márquez Pediatric Teaching Hospital and met the ethical guidelines of the Declaration of Helsinki.

Results

Characteristics of the sample

We studied 22 newborns with NS, 11 of which were male (50%). The mean gestational age was 37.98 weeks (SD 2.35, range 32.6-42), with four subjects (18.18%) premature (gestational age less than 37 weeks). The average birth weight was 2924 g (SD 582.68, interval 1802-3850), there were no cases with birth weight under 1500 g.

There were 12 eutocic births (54.54%), six cesarean sections (27.27%), and four deliveries with instruments (18.18%). The Apgar score at five minutes of life was less than 4 in two cases (9.09%).

Etiological Diagnosis

Table 1 shows the distribution of neonatal seizures according to etiology.

Electroencephalographic evaluations

The EEG behaved in the following way: 13.63% had normal EEG, 9.09% presented minimal alterations, 59.09% had moderate alterations, and 18.18% had serious alterations. **Figure 1** shows the electroencephalographic tracing of a patient who presented neonatal seizures before 24 hours of age.

Outcome

There were no deaths. In 40.9% (9/22) of the patients, a good outcome was observed. In the rest of the patients: epilepsy occurred in 40.9% (9/22), a delay in psychomotor development presented

in 9.09% (2/22), psychomotor development retardation plus epilepsy in 4.54% (1/22), and an infant cerebral palsy plus epilepsy in the remaining subject.

The analysis of the possible statistical associations showed statistically significant associations between the EEG result and the outcome of the patient ($p=0.015$), between gestational age and outcome ($p=0.003$), and between birth weight and outcome ($p=0.003$).

Seizures occurred in isolation (as the only risk factor) in 27.2%, associated with another risk factor in 18.1%, and with more than two risk factors in 53.7%.

Discussion

In the study, the most frequent cause of NS was hypoxic-ischemic encephalopathy coinciding with the results of other investigations.^{2,7-10} In relation to the etiology of seizures and the time of onset, some authors report that the majority of seizures that occur before the fifth day of life are usually due to hypoxic-ischemic encephalopathy, intracranial hemorrhage, metabolic disorders, CNS infection, or by the direct effect of drugs.^{2,11-13} Ninety percent of the seizures that appear in the course of hypoxia-ischemia occur within the first 48 hours of life. Seizures that manifest between 24-72 hours of life are due to CNS infections, drug withdrawal, hemorrhage, the onset of congenital errors in the metabolism, or brain malformations.^{2,8,14,15}

In this work, it is striking that the majority of NS occurred in full-term newborns (81.82%). A study by Sheth et al. analyzing the relationship between these two conditions found a parabolic distribution with a lower incidence between 30-36 weeks (4.8%) compared to the term group (11.9%).¹⁰

Moreover, the electroencephalographic alterations described in the group of patients who presented neonatal seizures in this study are similar to those reported by other authors^{2,6} highlighting that most of the patients presented moderate and severe

Table 1. Etiology of neonatal seizures

Etiology	N/%
HIE	10 / 45.45 %
ICH	4 / 18.18 %
CNS malformations	1 / 4.54 %
Metabolic	2 / 9.09 %
CNS infection	5 / 22.72 %

HIE: Hypoxic-Ischemic Encephalopath, ICH: Intracranial Hemorrhage, CNS: Central Nervous System

Figure 1. Pattern of surge suppression in newborn that begins with tonic spasms at 23 hours of birth.

alterations. Alcover also found that the recording of a pathological EEG (critical or with severe alterations) is associated with an unfavorable outcome in most cases.⁶ A more accurate prognosis in these patients can be attained from the etiology of neonatal seizures and electroencephalographic patterns.⁴

The persistence of pathological records beyond 72 hours of birth is invariably associated with death or serious neurological sequelae, while early recovery—before 12 or at least 36 hours—

is associated with normal results or with minor neurological alterations.¹⁶

The study by Jiménez *et al.* lists the presence of clinical neurological alterations during the first week of life, the presence of seizures, and a pathological EEG, as the main prognostic factors in perinatal asphyxia.¹⁷

Preterm children with an intercritical EEG within normality generally have a good prognosis, whereas

the EEG tracing of a “burst-suppression” in the neonatal period translates into a poor prognosis except when said tracing is of pharmacological origin.¹⁸

The EEG is very useful to confirm suspicions; however, it is not definitive for the diagnosis of NS. Conventional electroencephalography has a series of limitations in the study of these patients, among which are: a) difficulties in prolonged monitoring, b) excessive number of electrodes, c) electrical interference by surrounding equipment, d) difficulties in interpretation of the study requiring a staff trained in clinical neurophysiology, e) brief records (45-60 minutes) that even with periodic evaluations can lose information on the outcome of the alterations of the base activity, sleep states, and sporadic seizures. The incorporation of the amplitude-integrated EEG, a safe method for cerebral function monitoring, is a simple method of continuous recording of cortical electrical activity allowing to predict the final neurological outcome in as short a time as the first 6 hours of life.^{16,19}

The association between gestational age and birth weight is well known. Preterm newborns constitute a vulnerable population with a high risk of suffering medical problems and neurobehavioral disabilities^{20,21} including poor cognitive performance and greater learning difficulties, as well as an elevated risk of presenting behavioral disorders.

Of the total number of premature children, up to 47% of them present cerebral palsy, 27% show important cognitive disorders, and 23-37% have sensory disorders.^{22,23}

A study conducted by Salinas-Álvarez noticed that approximately three-quarters of their sample presented an overlap of risk factors. Their study of patients with high neurological risk describes that on a scale of one to ten risk factors, their sample had an average of 4.1.24 It has been described that these cases are more likely to develop a disability and that the accumulation of risks is not equivalent to a sum but that they are potentiated.

Conclusions

In patients with neonatal seizures, the etiology should be determined and confirmed by electroencephalographic evaluation; in turn, the result of the EEG could provide elements in the neurological prognosis of these children.

Conflicts of interest

The authors of the research state there are no conflicts of interest in this study.

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