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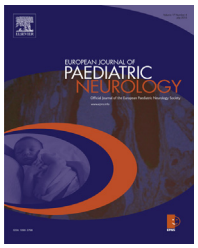

Original article

Neonatal seizures: Aetiology by means of a standardized work-up

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ABSTRACT

Neonatal seizures are an alarming symptom and are frequent in neonates. It is important to find the cause of neonatal seizures to start a specific treatment and to give a meaningful prognosis. The aim of this study is to investigate the incidence of different aetiologies of neonatal seizures in our hospital by a specific work-up.

Methods: All full-term born neonates from January 2002 till September 2009 with neonatal seizures, admitted to our neonatal intensive care unit were included ($n = 221$). Aetiology was investigated by means of a standardized aetiologic work-up.

Results: The frequencies of aetiologies of neonatal seizures were: hypoxic-ischemic encephalopathy (HIE) ($n = 119$; 53.9%), metabolic or electrolyte disorders ($n = 24$; 10.9%), intracranial hemorrhage ($n = 20$; 9.0%), ischemic infarction ($n = 16$; 7.2%), intracranial infections ($n = 14$; 6.3%), congenital malformations of the central nervous system ($n = 7$; 3.2%), inborn errors of metabolism ($n = 5$; 2.3%), epileptic syndromes ($n = 1$; 0.5%), HIE + hypoglycemia ($n = 4$; 1.8%), HIE + intracranial hemorrhage ($n = 3$; 1.4%), HIE + ischemic infarction ($n = 1$; 0.5%), ischemic infarction + intracranial hemorrhage ($n = 1$; 0.5%), idiopathic ($n = 4$, 1.8%), intoxications ($n = 1$; 0.5%) and unknown ($n = 1$; 0.5%).

Conclusion: Our work-up is a practical tool to find the aetiology of neonatal seizures.

1. Introduction

Neonatal seizures are an alarming symptom. The incidence of seizures is 1.8–2.8 per 1000 newborns.[1–5] Volpe[5] has made a classification of neonatal seizures into subtle, clonic, tonic and myoclonic.[5]

Recognition of neonatal seizures is difficult, and over-diagnosis happens frequently.[6] First, seizures should be

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distinguished from jitteriness[7,8] and benign sleep myoclonus[7,9,10]. Second, subtle seizures may be mimicked by the administration of morphine too and apneic spells usually have no epileptic origin according to Volpe.[5] However, during the neonatal period, apnea has been associated with epileptiform activity in the absence of posturing.[11] Therefore, unexplained apneic spells should be evaluated with an electroencephalogram (EEG). Third, both clinical[12,13] as subclinical seizures[12,14] may be present.

It is important to find the cause of neonatal seizures for starting a specific treatment and to give a meaningful prognosis. The aetiology can be divided into: hypoxic-ischemic encephalopathy (HIE), ischemic infarction, intracranial hemorrhage, intracranial infections, metabolic or electrolyte disorders, congenital malformations of the central nerve system (CNS), inborn errors of metabolism, intoxications and epileptic syndromes.

The aim of this study was to investigate the incidence of aetiologies of neonatal seizures in full-term neonates at the University Medical Center Groningen (UMCG), the Netherlands, by means of a work-up for neonatal seizures.[15] In addition we wanted to compare our results to literature.

2. Materials and methods

2.1. Study population

All full-term born neonates ($n = 315$) that were admitted to the neonatal intensive care unit (NICU) of the University Medical Center Groningen, the Netherlands, from January 2002 till September 2009 and who were suspected to have had neonatal seizures during the first 28 days after birth, were included. Immediately after admission, all neonates were monitored bed-side by amplitude integrated EEG (aEEG) for at least 48 h. The history of clinical seizures, the aEEG and the EEG results were used to confirm or to rule out the presence of seizures. Seizures were considered to be present in case of tonic and/or clonic movements and/or ictal activity at the aEEG and/or EEG. Both infants with clinical and subclinical seizures were included. Eventually, 221 newborns were diagnosed with neonatal seizures and were subsequently included in our study.

2.2. Methods

The aEEGs were recorded by the analog Lectromed® Multitrace 2 or the digital Olympic® CFM 6000. In case of the latter access to raw single-lead EEG was possible. If a full EEG was done, this was recorded for one hour.

To determine the aetiology of neonatal seizures relevant clinical information, laboratory results, aEEG/EEG, and imaging were obtained from our computerized hospital-based medical record system, retrospectively. If any information was lacking the original medical record was consulted. Information about pregnancy, delivery, Apgar scores, start and duration of the seizures, type of seizures, clinical presentation at admission, illness in the direct environment, family history, and dysmorphic features were obtained. Dysmorphic features were defined as congenital external abnormalities that may indicate a syndromal disorder or an inborn error of metabolism.[15] Table 1 shows different features of specific aetiologies for neonatal seizures. The combination of Fig. 1 and Table 2 represent the work-up that is used in our NICU in the diagnostic work-up of neonatal seizures. Fig. 1 represents the flowdiagram and in Table 2 the specific items of the diagnostic evaluation can be found. This evaluation is divided into elementary and extended evaluation. Elementary evaluation is based on the early detection of the most common and treatable causes of neonatal seizures and should always be performed in (suspected) neonatal seizures. In order to exclude diagnostic "mimics" for instance HIE, the first column of Tables 2 and 1 were used to decide whether or not the supposed aetiological diagnosis was compatible with the clinical presentation and the laboratory results. If not, extended evaluation was initiated. Furthermore, the extended evaluation was applied if the aetiology was still unknown or in case of persistent seizures. Table 2 also advises specific diagnostic tests which are conducted only in case of suspicion of certain diseases.

At discharge from the NICU the diagnosis was regularly not yet definite, because not all the results were yet available. Table 1, Table 2 and Fig. 1 in combination with the obtained information were used as a tool to define a final aetiology of the neonatal seizures. Table 3 shows the final aetiology. Idiopathic means that there is a suspicion of a genetic disorder, however, this cause can not be detected (yet). Unknown means that despite all evaluation done, no cause has been found without suspicion for a genetic disorder.

The study was approved by the ethics committee of the University Medical Center Groningen.

2.3. Statistics

Descriptive statistics were used.

3. Results

Two hundred twenty-one newborns were included; 57% boys and 43% girls. The mean gestational age was 39^{+4} weeks (range: 37–42) and the mean birth weight was 3490 g (range: 1910–5475). Sixty six newborns (29.9%) deceased before the end of the neonatal period and 33 newborns with neonatal seizures (14.9%) had a status epilepticus. EEG was performed in 181 cases (81.9%). Cerebral MRI was performed in 143 neonates (64.7%).

3.1. Aetiology of neonatal seizures

The aetiologies of neonatal seizures were: 119 HIE (53.9%), 24 metabolic or electrolyte disorders (10.9%), 20 intracranial hemorrhage (9.0%), 16 ischemic infarction or cerebral sinovenous thrombosis (7.2%), 14 intracranial infections (6.3%), 7 congenital malformations of the central nervous system (3.2%), 5 inborn errors of metabolism (2.3%), 1 epileptic syndromes (0.5%), 4 idiopathic (1.8%), 1 intoxications (0.5%) and 1 unknown (0.5%). Double diagnosis was present in nine newborns; 4 HIE + hypoglycemia (1.8%), 3 HIE + intracranial