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Assessment of the association between Apgar scores and seizures in infants less than 1 year old

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ABSTRACT

Purpose: The study aimed to assess the association between Apgar scores at 1 and 5 min after birth and seizures in infants less than 1 year old.
Methods: We conducted a retrospective, observational, hospital-based study by utilising medical records from the Chung-Ang University Hospital admissions from January 2006 to May 2015 in order to identify infants less than 1 year old who had a history of seizures. Using electronic medical records, infants who were diagnosed with infantile seizures at the Chung-Ang University Hospital from January 2006 to May 2015 were included in the seizure group (n = 93), and a control group consisting of 296 age-matched cases without a history of seizures was selected from a group of infants born at Chung-Ang University Hospital during the same study period.
Results: We found that Apgar scores were significant risk factors for infantile seizures. Apgar scores differed depending on gestational age and birth weight. We found strong associations between Apgar scores and infantile seizures in the full-term and the normal-birth weight groups (bodyweight $\geq$2.5 kg), regardless of delivery mode. The Apgar scores were inversely correlated with the EEG class, and only the 1-min Apgar scores were correlated with MRI findings.
Conclusion: Low Apgar scores are significant perinatal risk factors for infantile seizures, especially in full-term and normal-birth weight infants, and have a strong negative linear relationship with EEG and brain MRI results in the seizure group.

1. Introduction

The 10-point Apgar scale has been used to assess the physiologic condition and prognosis of new-born children throughout the world for over 60 years [1]. However, the use of the Apgar score has become controversial, because medical professionals have attempted to apply it as a prognostic indicator of an infant's neurodevelopment, a use for which it was not initially developed [1]. Since infantile seizures (seizures occurring at less than 1 year of age) are the most common and distinctive clinical manifestations of neurological dysfunction in an infant [2], it is therefore reasonable to assume that seizures at less than 1 year of age are related to the perinatal condition in ways that are not yet fully understood. The Apgar score is a widely used tool that reflects the overall perinatal condition of the newborn [3].

The aim of this study was to investigate the possibility of predicting the neurological prognosis of infants by analysing the correlation between the Apgar score and the incidence of infantile seizures. First, we sought to determine whether Apgar scores, among other routinely measured perinatal values, could significantly contribute to prediction of infantile seizures. Next, if the relationship with infantile seizures proved significant, our aim was to assess the strength of the association of Apgar scores with infantile seizures in terms of other perinatal values, including gestational age (GA) and birth weight. Finally, we analysed the correlation of Apgar scores with electroencephalogram (EEG) and brain magnetic resonance imaging (MRI) findings, from which we assessed the possibility of using Apgar scores as prognostic indicators of the neurodevelopmental status of infants less than 1 year old.

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2. Materials and methods

2.1. Study population

The study population ($n = 93$) was derived from infants treated at the Chung-Ang University Hospital between January 2006 and May 2015. Control group subjects ($n = 294$) were selected from infants born at the Chung-Ang University Hospital between January 2006 and May 2015, who were younger than 1 year of age and had no history of seizures, irrespective of the presence of other diseases, including all neurological disorders except seizure or epilepsy. The control group subjects were selected from infants whose onsets of chief complaints were as close as possible to the onset of each seizure case for randomisation after excluding age, to avoid the potential for bias.

2.2. Samples and sample size

Data collection occurred over a 6-month period. A total of 130 patients and 425 control subjects were recruited for the study. Thirty-seven patients and 129 control subjects with inadequate data for various reasons (i.e., refusal to participate [$n = 10$], inability to provide hospital records of birth on telephone inquiry [$n = 128$], or unreliable data [$n = 28$]) were excluded from the study. The final study population included 93 patients in the seizure group and 296 control subjects.

2.3. Definitions

Epilepsy was defined as the presence of two or more afebrile seizures that were not associated with an acute central nervous system (CNS) insult and did not occur within a 24-h period. Diagnostic criteria for hypoxic ischaemic encephalopathy (HIE) included evidence of foetal difficulty in the final hours before birth, depression at birth and the need for resuscitation, severe metabolic acidosis, neonatal clinical and imaging signs of acute neurological abnormalities, evidence of dysfunction of other systems and exclusion of other causes of neonatal encephalopathy [4]. Intracranial haemorrhage (ICH) included primary subarachnoid-haemorrhage, germinal matrix-intraventricular haemorrhage and subdural haemorrhage. Hypocalcaemia was defined as calcium levels <7 mg/dL in a blood sample. Neurodevelopmental disruption included agenesis of the corpus callosum, brain tumour, subarachnoid cyst and Dravet syndrome. Febrile seizures were defined as seizures occurring between the ages of 3 months and 6 years in patients with no previous afebrile seizures and associated with fever but without evidence of intracranial infection or other recognised acute neurological illness. CNS infection was identified in patients with meningitis or encephalitis consequent to an inflammatory cell response on lumbar puncture. A patient was diagnosed with convulsions with gastroenteritis when presenting with seizures accompanied by symptoms of gastroenteritis, without clinical signs of dehydration or electrolyte derangement, and a body temperature below 38.0 °C before and after the seizures [5]. Different seizure types were defined according to the published International League Against Epilepsy classification of seizures and Volpe's classification [6]. We considered Apgar scores between 1 and 6 as low and those between 7 and 10 as normal, in order to determine the odds ratio (OR). Based on the EEG wave analysis, we categorised all EEG findings into 4 subgroups: normal (0 on EEG), partial seizures (1 on EEG), generalised seizures (2 on EEG), and cerebral dysfunction (3 on EEG). EEG classifications were based on EEG findings within 24 h of seizure onset. Abnormal brain MRI findings included the presence of an arachnoid cyst, hippocampal sclerosis, encephalomalacia, intracranial haemorrhage, a tumorous lesion and microcephaly. MRI was obtained during hospitalisation, and additional MRI scans were not performed for further classification under the abnormal category. Mean age at MRI scanning was 118 ± 90 days (range, 2–360).

2.4. Data collection

Patient data collected included Apgar scores, sex, mode of delivery, GA, birth weight, EEG and brain MRI findings and seizure aetiology. The medical records of all patients who experienced clinically evident infantile seizures (i.e., seizure or convulsion within the first year of life, confirmed by a paediatric neurologist) were retrospectively reviewed. We collected the infants' Apgar scores and other perinatal data using electronic medical records (EMRs). If infants were born at another hospital but transferred to the Chung-Ang University Hospital for the treatment of seizures, we obtained their Apgar scores from the referring hospital via telephone inquiry.

2.5. Statistical analysis

A multiple logistic regression model was used to determine the most significant perinatal factor among known factors including sex, Apgar scores, birth weight, GA, mode of delivery, and mother's age. Significance was determined using ORs with 95% confidence intervals (95% CIs). The 1- and 5-min Apgar scores were compared between the seizure and the control groups, between sexes, and among modes of delivery using independent t-tests. The comparison of Apgar scores among GA and birth weight groups was performed using the Kruskal–Wallis and Mann–Whitney U tests. The strength of the correlation of Apgar scores with modes of delivery, GA, and birth weight in both groups was analysed using the chi-square and Mantel–Haenszel methods. We used a bivariate correlation analysis to determine the correlation between Apgar scores and EEG findings, and the chi-square test to determine the correlation between Apgar scores and MRI findings. All P-values were derived from the two-sided test, and $P < 0.05$ was considered statistically significant. All analyses were performed using the PASW Statistics ver. 18.0 (SPSS Inc., Chicago, IL, USA) software.

3. Results

3.1. General characteristics of seizures

Ninety-three cases of infantile seizures were included in the seizure group. The aetiology of seizures included HIE ($n = 18$, 19.4%), hypocalcaemia ($n = 12$, 12.9%), ICH ($n = 11$, 11.8%), brain anomaly ($n = 7$, 7.5%), convulsion with gastroenteritis ($n = 4$, 4.3%), febrile seizure ($n = 4$, 4.3%), CNS infection ($n = 1$, 1%) and unknown causes ($n = 35$, 37.5%). The 1- and 5-min Apgar scores (mean $\pm$ SD) varied according to aetiology (HIE: 5.17 ± 2.70, and 6.83 ± 2.46, respectively; ICH: 6.27 ± 1.85 and 8.09 ± 1.14; hypocalcaemia: 7.33 ± 1.37 and 8.58 ± 1.08; brain anomaly: 7.57 ± 1.13 and 9.14 ± 0.38; convulsion with gastroenteritis: 8 and 9; CNS infection: 8 and 9; febrile seizure: 8 and 9; and unknown causes: 7.94 ± 0.73 and 8.83 ± 0.79). The onset of seizures (days $\pm$ SD from birth) also varied according to aetiology (CNS infection: 1; HIE: 2.73 ± 3.40; ICH: 9.44 ± 15.10; metabolic causes: 13.70 ± 28.02; convulsion with gastroenteritis: 132 ± 134; brain anomaly: 175 ± 136; febrile seizures: 220 ± 131; and unknown causes 83.09 ± 96.70).

Of the 93 patients presenting with seizures, the seizure types were classified as follows: atonic, ($n = 1$:1 infant); focal clonic ($n = 7$:4 neonates, 3 infants); focal tonic ($n = 3$:1 neonate, 2 infants); generalised tonic ($n = 17$:9 neonates, 8 infants); generalised tonic clonic ($n = 33$:18 neonates, 15 infants); multifocal clonic ($n = 4$:3 neonates, 1 infant); multifocal myoclonic ($n = 2$:2 neonates); and subtle ($n = 18$:15 neonates, 3 infants).