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***Retrospective Study***

**Clinical and electroencephalogram characteristics and treatment outcomes in children with benign epilepsy and centrotemporal spikes**

Chen RH *et al*. EEG characteristics and treatment outcomes in BEC

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**Abstract**

BACKGROUND

Epilepsy is a syndrome characterized by transient, rigid, paroxysmal, and repetitive central nervous system dysfunction. Prevention, control, and improvement of cognitive and behavioral dysfunction are of great significance for improving the patients’ intellectual development and quality of life. Electroencephalograms (EEG) can predict an accelerated decline in cognitive function.

AIM

To determine the clinical and EEG characteristics and treatment results of benign epilepsy in spiking children.

METHODS

A total of 106 cases of benign epilepsy in children with myocardial spines treated at our hospital from January 2017 to January 2020 were selected. Differences in clinical data and EGG characteristics between treatment-effective/-ineffective patients were analyzed, and children’s intellectual development before and after treatment evaluated using the Gesell Development Diagnostic Scale.

RESULTS

EEG showed that the discharge proportion in the awake and sleep periods was 66.04%, and the peak/peak discharge was mainly single-sided, accounting for 81.13%, while the discharge generalization accounted for 31.13%. There was no significant difference in any of these variables between sexes and ages (*P* > 0.05). The proportion of patients with early onset (< 5 years old) and seizure frequency > 3 times/half a year was 40.00% and 60.00%, respectively; the incidence rate and seizure frequency in the younger age group (< 5 years old) were significantly higher than those in the treatment-effective group (*P* < 0.05), while the discharge index was significantly lower than that in the treatment-effective group (*P* < 0.05). The discharge index was negatively correlated with fine motor skill and language development (*r* = -0.274 and -0.247, respectively; *P* < 0.05), but not with the rest (*P* > 0.05). Logistic regression analysis showed that low age onset (< 5 years old) and seizure frequency were the factors affecting ineffective-treatment of benign epilepsy in children (odds ratio = 11.304 and 5.784, respectively; *P* < 0.05). The discharge index of the responsive group after treatment was significantly lower than that of the unresponsive group (*P* < 0.05). However, there was no significant difference between groups after treatment in gross and fine motor skills, adaptability, language, and personal social development (*P* > 0.05).

CONCLUSION

The EEG of children with benign epilepsy due to spinal wave in central time zone has characteristic changes, and the therapeutic effect is influenced by age of onset and attack frequency.

**Key Words:** Centrotemporal spikes; Benign epilepsy; Children; Electroencephalogram; Therapeutic effect

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**Core Tip:** The electroencephalogram of children with benign epilepsy with centrotemporal spikes has characteristic changes, and the therapeutic effect is affected by the age and attack frequency of the children at the time of onset.

**INTRODUCTION**

Epilepsy is a syndrome characterized by transient, rigid, paroxysmal, and repetitive central nervous system dysfunction, generally caused by excessive neuron synchronization in the brain and self-limited abnormal discharge caused by various etiological factors. As a common disease among children, the incidence rate of epilepsy has shown an increasing trend in recent years. Benign epilepsy in children with centrotemporal spike waves is an age-dependent epileptic syndrome, which generally peaks between 6–8 years old, with normal mental and motor development[1,2]. At present, the primary goal of antiepileptic treatments is to completely control epileptic seizures, while simultaneously considering prevention, control, and improvement of cognitive and behavioral dysfunction is of great significance for improving the patients’ intellectual development and quality of life. Electroencephalogram (EEG) is an important external validator of normal brain structure and function and useful to detect some brain alterations. Cognitive function, an important aspect of brain function, is also based on brain morphology and/or function. Studies have shown that abnormal EEG can predict an accelerated decline in cognitive function[3,4]. In this study, the clinical and EEG characteristics of children with benign epilepsy and centrotemporal spikes were analyzed, and the children’s treatment and outcomes also discussed.

**MATERIALS AND METHODS**

***Patients***

A total of 106 cases of benign epilepsy, including 66 males and 40 females, in children with spinous waves in the central temporal region were treated at our hospital from January 2017 to January 2020. Their ages ranged from 3 to 12 years old, and their average age was 7.15 ± 1.82 years old. The inclusion criteria were: (1) The diagnosis met the criteria for the epilepsy diagnosis and treatment guidelines of the International League Against Epilepsy; (2) first-time treatment; (3) aged 3–12 years old; (4) complete clinical, EEG, and follow-up data; (5) had intelligence tests; and (6) informed consent from the child’s guardian. The exclusion criteria were: (1) A history of encephalitis, meningitis, brain developmental malformation, and other brain diseases; (2) other diseases such as connective tissue disease, nephrotic syndrome, and immunodeficiency; and (3) patients with a history of glucocorticoid and other treatments within 6 mo before treatment in our hospital.

***Treatment and follow-up***

The children were treated with levetiracetam and lamotrigine. The levetiracetam dose was 10 mg/kg/d, and the final therapeutic dose was 10-30 mg/kg/d. Lamotrigine was administered at doses from 0.3-0.6 mg/kg/d, gradually increasing to 3-6 mg/kg/d. Each child was followed for 1 year after treatment, and the treatment was considered ineffective if there were clinical epileptic seizures during the follow-up period, and effective if there were no clinical epileptic seizures.

***EEG examination***

We employed an EEG-1200C manufactured by Japan Optoelectronics Co., Ltd with the following parameters: Gain, 50 µV; high-pass filtering conducted at 45 Hz; time constant, 0.3 s; accuracy, 16 bit; frequency, 200 Hz; and scalp resistance, ≤ 5000 MΩ. Reference electrodes were placed on the bilateral earlobes and we used 16 recording electrodes in total. EEG signals were recorded in a quiet and eye-closed state for 5 min, and the complexity was calculated. The human electroencephalogram frequency was (0.5-30) Hz, including β (13.5-30.0) Hz, α (8.0–13.0) Hz, θ (4.0-7.5) Hz, and δ (1.0-3.5) Hz.

***Intelligence development test***

The development of children’s intelligence was assessed using the Gesell Development Diagnostic Scale, which included five domains, namely, gross motor, fine motor, adaptability, language, and personal-social ability. The test result of each domain is expressed as development quotient (DQ), and a DQ > 85 was considered normal.

***Statistical analysis***

SPSS22.0 software was used for data analyses. Measurement data with a normal distribution are expressed as the mean ± SD, and *t* test was used for comparison between groups. Count data are expressed as *n* (%), and inter-group comparisons were performed by the chi-square test. Pearson correlation analysis for correlation, and logistic regression analysis for multivariate analysis were also performed. *P* values < 0.05 were considered statistically significant.

**RESULTS**

***Children's EEG characteristics***

Among the 106 children, the EEG showed a discharge proportion in the awake and sleep periods of 66.04%, a spike/sharp wave discharge rate of 81.13% (mainly unilateral discharge), and a discharge generalization rate of 31.13%, as shown in Table 1.

***Comparison of children’s EEG characteristics with respect to sex and age***

There was no significant difference in the proportion of discharge, spike/sharp wave unilateral discharge, and discharge generalization between the sexes and among all age groups either during the awake or asleep period (*P* > 0.05), as shown in Table 2.

***Comparison of clinical data of treatment responsive/unresponsive children***

The proportion of children with young-age onset (< 5 years old) and attack frequency > 3 times/half a year in the treatment unresponsive group was significantly higher than that in the treatment responsive group (*P* < 0.05), and the discharge index significantly lower (*P* < 0.05). There was no significant difference in sex, age, or discharge period between the treatment responsive/unresponsive groups (*P* > 0.05, Table 3).

***Correlation between discharge index and Gesell scale***

Pearson correlation analysis showed a negative correlation between the discharge index and fine motor skills and the language development quotient (*r* = − 0.274 and − 0.247, respectively; *P* < 0.05), but no significant correlation was observed in any other parameters (*P* > 0.05), as shown in Table 4 and Figure 1.

***Results of multivariate analysis***

Logistic regression analysis was performed using the above statistically significant indicators as independent variables and treatment effectiveness as the dependent variable. The results showed that low age (< 5 years old) and seizure frequency were the factors affecting the lack of treatment response in children with benign epilepsy and centrotemporal spike wave (Odds ratio = 11.304 and 5.784, respectively; *P* < 0.05), as shown in Table 5.

***Comparison of discharge index and Gesell scale between treatment responsive/unresponsive children before and after treatment***

The discharge index after treatment in the treatment responsive group was 34.47 ± 10.02%, significantly lower than that in the unresponsive group (*P* < 0.05). In the treatment responsive group, fine motor skills, adaptability, and language development quotient improved after treatment (*P* < 0.05). There was no significant difference in gross and fine motor skills, adaptability, language, or personal-social ability development quotient between the treatment responsive/unresponsive group after treatment (*P* > 0.05, Table 6).

**DISCUSSION**

Epilepsy is a brain disease mainly characterized by transient central nervous system dysfunction caused by abnormal neuron discharge. Repeated epileptic seizures are often accompanied by a variety of neurobiological, cognitive, psychological, and social dysfunctions. Benign epilepsy with spinous waves in the central temporal region is the most common partial epilepsy in childhood, with an onset age between 3-13 years and accounting for 15%-24% of all kinds of epilepsy in children[5]. Several studies have shown that children with epilepsy and centrotemporal spikes have various degrees of cognitive and behavioral damage[6,7], while other reports have found that the cognitive impairment in these children is not caused by seizures but related to frequent clinical discharge. Neuropsychological and sociological problems exist in half of these children after adulthood[8,9]. Although the primary goal of antiepileptic treatment is to completely control epileptic seizures, prevention, control, and improvement of cognitive and behavioral dysfunction must be simultaneously considered. Therefore, clinicians must achieve a balance between controlling the epileptic seizures as much as possible and preserving cognitive and behavioral functions[10]. Long-term outbreaks of spike-and-slow wave rhythm and bilateral asynchronous spike-and-slow wave distribution cause more severe cognitive impairment than single spike waves[11]. EEG monitoring, a common modern auxiliary examination method for the clinical diagnosis of mild cognitive impairment diseases, induces no physical trauma and has confirmed value in the diagnosis of brain diseases. However, comprehensive analyses, as well as other experimental and auxiliary examinations, need to be conducted based on specific symptoms and signs; therefore, it is of great clinical significance to explore chemical markers of brain damage[12]. EEG represents the waveforms formed by the brain spontaneous potential; these waveforms can be divided into α, β, γ, θ, and δ waves according to their frequencies, with different waveforms being shown at different ages, in various consciousness states, and at various brain function levels[13,14]. Some studies have shown that abnormal EEGs can predict an accelerated decline in cognitive function. In children with epilepsy, EEGs accompanied by spinous waves in the central temporal region during the attack stage are often characterized by tonic-clonic seizures, where the initial fast wave activity of low amplitude in the central or middle temporal region on one side gradually increases in amplitude and decreases in frequency, gradually evolving into the alternating appearance of spinous and slow waves, which can be generalized to the ipsilateral hemisphere or even spread to the contralateral one[15]. At present, EEGs are considered to be highly related to epilepsy with spinous waves in the central temporal region. And compared with those of healthy peers, an increase in extremely high-amplitude spinous and slow waves in the high Rolandic region can be observed in the awake period, along with a widespread rhythmic outbreak of 2-3 Hz high-amplitude spinous and slow waves in the awake period. However, the discharge is significantly increased in the sleep period, and the spinous and slow wave discharge index is > 50% during the non-rapid-eye-movement sleep period[16]. In epilepsy accompanied by centrotemporal spikes, the presence of a status epilepticus EEG during sleep is known to cause nerve damage and cognitive changes; the higher the abnormal discharge index in the EEG, the more severe the cognitive damage in children. Therefore, we should actively diagnose, treat, and observe the therapeutic effects in children with epilepsy accompanied by centrotemporal spikes[17,18]. In this study, correlation analysis revealed that the discharge index was negatively correlated with fine motor performance and the language development quotient. Logistic regression analysis showed that an early age of onset (< 5 years old) and seizure frequency were influencing factors for the unresponsive treatment of benign epilepsy with centrotemporal spikes in children, indicating that monitoring the EEG discharge index could be used to preliminarily determine the children’s fine motor skills and language development quotient. During treatment, great attention should be given to children with early-onset and frequent seizures in whom clinical treatment has a poor effect. Frequent attacks can lead to delayed reaction time or even reaction loss in children, suggesting that abnormal discharges may be accompanied by transient cognitive function changes under clinical conditions, which reminds us that seizure control should not be the target of clinical treatment but the inhibition of clinical discharge and subsequent improvement in patients’ cognitive function[19,20]. An early age of onset is an important factor leading to poor treatment effect in children with benign epilepsy and centrotemporal spikes. Given the lack of clear clinical data on the specific scope of early-onset benign epilepsy with centrotemporal spikes, an early age at onset can be used as a relevant factor to predict treatment prognosis in these children. In this study, early age of onset was < 5 years old.

The analysis of the results of this study showed that the two antiepileptic drugs levetiracetam and lamotrigine could effectively control epileptic seizures and inhibit epileptic discharge, thus improving children’s cognitive function. However, this study has various limitations. Due to the limited number of enrolled children, there may be some deviation and error in the evaluation of discharge index, which may lead to a lack of generalizability. Therefore, further research expanding the sample size and extending follow-up time is needed.

**CONCLUSION**

In summary, the EGG of children with benign epilepsy and centrotemporal spikes has characteristic changes, and therapeutic effects are affected by the age and attack frequency at the time of onset.

**ARTICLE HIGHLIGHTS**

***Research background***

The primary goal of antiepileptic treatments is to completely control epileptic seizures, while simultaneously considering prevention, control, and improvement of cognitive and behavioral dysfunction is of great significance for improving the patients’ intellectual development and quality of life.

***Research motivation***

In this study, the clinical and electroencephalograms (EEG) characteristics of children with benign epilepsy and centrotemporal spikes were analyzed, and the children’s treatment and outcomes also discussed.

***Research objectives***

This study aimed to determine the clinical and EEG characteristics and treatment results of benign epilepsy in spiking children.

***Research methods***

A total of 106 benign epilepsy children with myocardial spines were included. Differences in clinical data and EGG characteristics between treatment-effective/-ineffective patients were analyzed, and children’s intellectual development before and after treatment evaluated using the Gesell Development Diagnostic Scale.

***Research results***

EEG showed that the discharge proportion in the awake and sleep periods was 66.04%, and the peak/peak discharge was mainly single-sided, accounting for 81.13%, while the discharge generalization accounted for 31.13%. The discharge index was negatively correlated with fine motor skill and language development, but not with the rest. The discharge index of the responsive group after treatment was significantly lower than that of the unresponsive group.

***Research conclusions***

The EGG of children with benign epilepsy and centrotemporal spikes has characteristic changes, and therapeutic effects are affected by the age and attack frequency at the time of onset.

***Research perspectives***

Further research expanding the sample size and extending follow-up time is needed.

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**Footnotes**

**Institutional review board statement:** This study was approved by the Ganzhou Maternal and Child Health Hospital Medical Ethics Committee.

**Informed consent statement:** All study participants, or their legal guardian, provided informed written consent prior to study enrollment.

**Conflict-of-interest statement:** This is no conflict of interest to disclose.

**Data sharing statement:** No additional data are available.

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**Figure Legends**



**Figure 1 Correlation analysis.** A: Fine motion; B: Language.

**Table 1 Electroencephalogram characteristics of children**

|  |  |  |
| --- | --- | --- |
| **Electroencephalogram characteristic** | **Number of cases** | **Proportion (%)** |
| Discharge period |  |  |
| Awake and sleep periods | 70 | 66.04  |
| Sleep period | 36 | 33.96  |
| Spine/spike discharge |  |  |
| Unilateral | 86 | 81.13  |
| Bilateral | 20 | 18.87  |
| Discharge generalization | 33 | 31.13  |

**Table 2 Comparison of electroencephalogram characteristics of children of different sexes and ages**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Group** | **Number of cases** | **Awake and sleep discharge (%)** | **Spike/sharp wave unilateral discharge (%)** | **Discharge generalization (%)** |
| Gender |
| Man | 66 | 42 (63.64) | 55 (83.33) | 19 (28.79) |
| Woman | 40 | 28 (70.00) | 31 (77.50) | 14 (35.00) |
| *χ*2 |  | 0.450  | 0.554  | 0.448  |
| *P* value |  | 0.502  | 0.457  | 0.503  |
| Age |
| ≤ 7 yr | 34 | 25 (73.53) | 26 (76.47) | 11 (32.35) |
| > 7 yr | 72 | 45 (62.50) | 60 (83.33) | 22 (30.56) |
| *χ*2 |  | 1.253 | 0.711 | 0.035 |
| *P* value |  | 0.263 | 0.399 | 0.852 |

**Table 3 Comparison of clinical data of children with and without effective treatment, *n* (%)**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Clinical data** | **Treatment ineffective (*n* = 20)** | **Treatment effective (*n* = 86)** | ***t*/*χ*2** | ***P* value** |
| Gender |  |  | 0.554 | 0.457 |
| Man | 11 (55.00) | 55 (63.95) |  |  |
| Woman | 9 (45.00) | 31 (36.05) |  |  |
| Age (yr) | 7.15 ± 1.98 | 7.15 ± 1.80 | 0.000 | 1.000 |
| Discharge period |  |  | 0.883 | 0.347 |
| Awake and sleep periods | 15 (75.00) | 55 (63.95) |  |  |
| Sleep period | 5 (25.00) | 31 (36.05) |  |  |
| Spike/sharp wave discharge |  |  | 2.081 | 0.149 |
| Unilateral | 19 (95.00) | 67 (77.91) |  |  |
| Bilateral | 1 (5.00) | 19 (22.09) |  |  |
| Discharge generalization | 8 (40.00) | 25 (29.07) | 0.904 | 0.342 |
| Low age onset (< 5 yr) | 8 (40.00) | 6 (6.98) | 12.690 | 0.000 |
| Seizure frequency |  |  | 9.582 | 0.002 |
| > 3 times/half a year | 12 (60.00) | 21 (24.42) |  |  |
| ≤ 3 times/half a year | 8 (40.00) | 65 (75.58) |  |  |
| Discharge index (%) | 65.05 ± 7.74 | 73.28 ± 9.17 | -3.714  | 0.000  |
| Gesell scale |  |  |  |  |
| Gross motor (points) | 85.70 ± 6.62 | 85.28 ± 7.29 | 0.236  | 0.814  |
| Fine motor (points) | 88.60 ± 5.99 | 86.62 ± 8.00 | 1.040  | 0.301  |
| Adaptability (points) | 87.60 ± 7.02 | 86.08 ± 7.20 | 0.854  | 0.395  |
| Language (points) | 88.15 ± 7.13 | 86.33 ± 7.92 | 0.942  | 0.348  |
| Individual-social ability (points) | 85.40 ± 8.61 | 85.99 ± 8.22 | -0.287  | 0.775  |

**Table 4 Results of correlation analysis**

|  |  |
| --- | --- |
| **Gesell scale** | **Discharge index** |
| ***r*** | ***P* value** |
| Gross motor | -0.014 | 0.887 |
| Fine motor | -0.274 | 0.005 |
| Adaptability | -0.068 | 0.488 |
| Language | -0.247 | 0.011 |
| Individual-social ability | 0.098 | 0.316 |

**Table 5 Results of multivariate analysis**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Index** | **β** | **SE** | **Wals** | ***P* value** | **OR (95%CI)** |
| Incidence at a young age (< 5 yr) | 2.425 | 0.696 | 12.131 | 0.000 | 11.304 (2.888-44.251) |
| Attack frequency | 1.755 | 0.593 | 8.760 | 0.003 | 5.784 (1.809-18.490) |
| Constant term | -2.686 | 0.480 | 31.254 | 0.000 | - |

OR: Odds ratio.

**Table 6 Comparison of discharge index and Gesell scale scores between treatment-effective and treatment-ineffective children before and after treatment**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Index** | **Treatment ineffective (*n* = 20)** | **Treatment effective (*n* = 86)** | ***t*** | ***P* value** |
| Discharge index (%) |  |  |  |  |
| Before treatment | 65.05 ± 7.74 | 73.28 ± 9.17 | -3.714  | 0.000  |
| After treatment | 40.15 ± 5.36 | 34.47 ± 10.02 | 2.449  | 0.016  |
| *t* | 11.828  | 26.498  |  |  |
| *P* value | 0.000  | 0.000  |  |  |
| Gross motor (points) |  |  |  |  |
| Before treatment | 85.70 ± 6.62 | 85.28 ± 7.29 | 0.236  | 0.814  |
| After treatment | 85.90 ± 5.47 | 86.20 ± 6.47 | -0.192  | 0.848  |
| *t* | -0.104  | -0.875  |  |  |
| *P* value | 0.918  | 0.383  |  |  |
| Fine motor (points) |  |  |  |  |
| Before treatment | 88.60 ± 5.99 | 86.62 ± 8.00 | 1.040  | 0.301  |
| After treatment | 91.20 ± 2.69 | 89.24 ± 5.29 | 1.605  | 0.111  |
| *t* | -1.771  | -2.533  |  |  |
| *P* value | 0.085  | 0.012  |  |  |
| Adaptability (points) |  |  |  |  |
| Before treatment | 87.60 ± 7.02 | 86.08 ± 7.20 | 0.854  | 0.395  |
| After treatment | 88.50 ± 5.04 | 88.26 ± 5.38 | 0.182  | 0.856  |
| *t* | -0.466  | -2.249  |  |  |
| *P* value | 0.644  | 0.026  |  |  |
| Language (points) |  |  |  |  |
| Before treatment | 88.15 ± 7.13 | 86.33 ± 7.92 | 0.942  | 0.348  |
| After treatment | 89.35 ± 6.02 | 88.55 ± 5.99 | 0.537  | 0.592  |
| *t* | -0.575  | -2.073  |  |  |
| *P* value | 0.569  | 0.040  |  |  |
| Personal-social ability (points) |  |  |  |  |
| Before treatment | 85.40 ± 8.61 | 85.99 ± 8.22 | -0.287  | 0.775  |
| After treatment | 86.95 ± 6.78 | 87.91 ± 6.27 | -0.607  | 0.545  |
| *t* | -0.633  | -1.722  |  |  |
| *P* value | 0.531  | 0.087  |  |  |