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Original article

# First-drug treatment failures in children with typical absence epilepsy

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**Abstract**

*Background:* Childhood absence epilepsy (CAE) is a well-known syndrome with onset in middle childhood and is characterized by multiple typical absences per day. Pharmacological treatment is specific and usually successful with a single medication. The goal of the study was to assess on risk factors associated with failure to respond to the initial antiepileptic drug (AED).

*Methods:* Fifty-two children with CAE were enrolled. Predictive factors were analyzed by survival methods.

*Results:* Among 52 patients, 32 patients (61.5%) were girls and the remaining 20 (38.5%) were boys and the mean age at the seizure onset was $6.5 \pm 1.78$ years old (3–11.5 years). Of the 52 patients, 42 (80.8%) were treated relatively successfully with the first AED treatment (Group A), and 10 (19.2%) were not responsed (Group B). Age of seizure onset, coexisting other types of seizures, and photoconvulsive EEG response were significantly associated with failure risk according to univariate analysis. In the multivariate analysis, only photoconvulsive EEG response was the risk factor influencing poor response to initial AED treatment.

*Conclusion:* Factors predicting failure to respond to the AED were age of seizure onset, coexisting other types of seizures, and photoconvulsive EEG response in children with CAE.


*Keywords:* Childhood absence epilepsy; First antiepileptic drug; Failure risk factors or predicting factors; Photoconvulsive EEG response

## 1. Introduction

Absence seizures are characterized by an abrupt cessation of activity, change in facial expression, impairment of consciousness, eye fluttering and sometimes associated by automatisms. As defined by the International League Against Epilepsy (ILAE) criteria, childhood absence epilepsy (CAE) is defined as typical absence seizures beginning under the age of ten, with an EEG discharge of symmetrical, synchronous spike wave complexes, recurring regularly at a rhythm of about 3 Hz [1]. Childhood absence epilepsy accounts for 10% to 17% of childhood epilepsy and usually presents between ages 4 and 8 [1,2].

Typical absence seizures may occur many times a day usually not surpassing 30 s induration. The end of the attack is as sudden as its onset, often with the child unaware of the seizure. The prevalence of typical absence seizures is highest during the first decade of life and then drops dramatically [3].

Treatment response to initial monotherapy is suboptimal, with slightly more than half of children achieving complete seizure control with acceptable treatment associated side effects.

In literature, only a few studies are available on factors associated with initial poor response to antiepileptic drugs (AED) [4–6]. Therefore, we conducted a retrospective study designed to identify the risk factors associated with initial poor response to AEDs in children with CAE.

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## 2. Subjects and methods

This study was conducted a retrospective study of 52 children diagnosed with CAE and started on an AED in the pediatric neurology department of our hospital.

Patients were selected based on the following inclusion criteria: (a) age from 3 to 13 years; (b) diagnosed typical absence seizures (ILAE Commission, 1981) [1] associated with generalized, synchronous 3-Hz (2.5–4 Hz) spike and wave activity, lasting >3 s, occurring spontaneously or during one of two trials of 3 min hyperventilation with a 1–2 min rest between trials; (c) clearly observable clinical signs of typical absence seizures (e.g., staring or impairment of consciousness); (d) treated with AEDs for the first time; (e) normal clinical, neurologic, and computed tomography (CT)/magnetic resonance imaging (MRI) examination.

The data were retrospectively collected from the clinic files and included sex, age of seizure onset, consanguinity, history of neonatal and febrile seizure, family history of epilepsy, coexisting other types of seizures, time lag to first treatment, electroencephalogram (EEG) findings (spike wave type and photoconvulsive response). Photoconvulsive response was defined as generalized epileptic discharge that was elicited during photic stimulation.

Success of initial AED was defined as obtaining complete seizure control with the first AED. Failure of initial AED treatment was defined as inability to attain complete seizure control with the first appropriate AED.

The SPSS version 19.5 was used for statistical analysis. Statistical significance was accepted at $p < 0.05$. The chi-square tests were used to determine the associations among categorical data. We carried out univariate and multivariable analyses of potential predictors of recurrence risk using by Cox regression analysis. The level of statistical significance was established at $p$- value of <0.05. Initially, we performed a univariate analysis, in order to determine which would used in multivariate analysis.

## 3. Results

The general characteristics of children treated with initial AED and factors for success and failure to the first AED are shown in Table 1.

Fifty-two children, mean age $7.50 \pm 1.67$ years (4–12.5 years), were included in this study. Among the 52 patients, 20 (38.5%) were boys and 32 (61.5%) were girls, and the mean age at the seizure onset was $6.50 \pm 1.78$ years (3–11.5 years).

Of the 52 patients, 42 (80.8%) were treated relatively successfully with the first AED (Group A), and 10 (19.2%) did not responsed to initial AED treatment (Group B).

Two patients (3.8%) had past history of febrile convulsion, and thirteen patients (25.0%) had family history of convulsive disorders. Twelve patients had coexisting other types of seizures: 10 patients (83.3%) had

Table 1
Summary of demographics and factors associated with success or failure of the first AED.

| Parameters | | Responders | | Non-responders | | P1 | P2 |
|---|---|---|---|---|---|---|---|
| | | *n* | % | *n* | % | | |
| Sex | Boy | 17 | 85.0 | 3 | 15.0 | 0.408 | |
| | Girl | 25 | 78.1 | 7 | 21.9 | | |
| Neonatal seizure | Yes | 0 | 100 | 0 | 0 | | |
| | No | 52 | 100 | 0 | 0 | | |
| History of febrile seizure | Yes | 1 | 50.0 | 1 | 50.0 | 0.351 | |
| | No | 41 | 82.0 | 9 | 18.0 | | |
| Consanguinity | Yes | 11 | 78.6 | 3 | 21.4 | 0.545 | |
| | No | 31 | 81.5 | 7 | 18.5 | | |
| Family history of epilepsy | Yes | 8 | 61.5 | 5 | 38.5 | 0.057 | |
| | No | 34 | 87.1 | 5 | 12.9 | | |
| Age of seizure onset | <5 years | 10 | 62.5 | 6 | 37.5 | **0.035** | **0.139** |
| | 5–10 years | 31 | 91.1 | 3 | 8.9 | | |
| | >10 years | 1 | 50.0 | 1 | 50.0 | | |
| Coexisting other types of seizures | Yes | 7 | 58.3 | 5 | 41.7 | **0.039** | 0.743 |
| | No | 35 | 87.5 | 5 | 22.5 | | |
| Focal spike activity on EEG | Yes | 6 | 85.7 | 1 | 14.3 | 0.519 | |
| | No | 36 | 80.0 | 9 | 20.0 | | |
| Photoconvulsive EEG response | Yes | 2 | 40.0 | 3 | 60.0 | **0.043** | **0.027** |
| | No | 40 | 85.1 | 7 | 14.9 | | |
| Time lag to first treatment | 1 month | 14 | 87.5 | 2 | 22.5 | 0.228 | |
| | 1–6 months | 19 | 82.6 | 4 | 27.4 | | |
| | >6 months | 9 | 69.2 | 4 | 30.8 | | |

P1: $p$ value of univariate analysis.
P2: $p$ value of multivariate analysis.