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Original article

Efficacy and tolerability of levetiracetam in children with epilepsy

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Abstract

Objective: To assess the efficacy and tolerability of levetiracetam (Lev) in children with epilepsy. *Methods:* Open-label observational, prospective, single arm, non-interventional study examining patients (⩽14 years) with epilepsy, receiving mono- or combination therapy with levetiracetam. Levetiracetam was started at a dose of approximately 10 mg/kg/day. The dose was titrated up with 10 mg/kg increments if seizures were poorly controlled but the maximum daily dose could not be more than 60 mg/kg/day. Documented were seizure type and frequency, levetiracetam dose and side effects. *Results:* 120 patients (39.3% females, mean age 4.5 ± 3.9 years) were enrolled. Average duration of follow-up was 10.3 ± 3.5 months. At study endpoint, 64.8% of patients got seizure free and 83.0% got a seizure reduction of ⩾50%. Observed side effects were somnolence, dysphoria, nervousness, dystrophy, somnipathy, asitia, debilitation, etc. and the incidence rate in the study was 47.5%. Four (3.3%) of 120 patients withdrew because of intolerance of side effects. The estimated one year retention rate of levetiracetam was 73.3%. Poor effect was the most common reason for withdrawal. *Conclusions:* In our study, it seemed that levetiracetam was safe and effective for a wide range of epileptic seizures in children with epilepsy.

Keywords: Levetiracetam; Efficacy; Side effects; Retention rates; Epilepsy

1. Introduction

The treatment of children with epilepsy is different from adults. For children, it is more important to choose AEDs with conspicuous efficacy, slight side effects and good compliance.

At present, there has been less experience in use of AEDs in children than that in adults. The proposition of use of AEDs in children is just simple extension from the studied in adults [1]. So more studied of AEDs for children are needed.

Levetiracetam (LEV, Keppra®) is a new AED with almost perfect pharmacokinetic profile [2,3]: about 100% bioavailability, less than 48 h to steady state, linear kinetics, twice-daily dosing, protein binding less than 10%, no hepatic metabolism, minimal metabolism in blood, no significant interactions with other AEDs. It has been recently licensed for treatment of children with partial epilepsy and of drug-resistant myoclonic seizures in juvenile myoclonic epilepsy [4,5]. The results of the placebo-controlled studies leading to approval and the open-label extension studies indicate that LEV constitutes a considerable progress in the treatment of epilepsy [6–8].

This open-label, prospective, single arm, non-interventional study is to assess the efficacy and tolerability of levetiracetam in children with epilepsy.

2. Materials and methods

The study is an open-label, prospective and community-based trial of levetiracetam (LEV) as therapy in children with epilepsy. This article reports the study results of the patients recruited for the study.

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2.1. Patients

Children consistent with the following conditions could be enrolled:

(1) Aged less than or equal to 14 years.
(2) Having a history of definite epileptic seizures with typical epileptiform discharge in their electroencephalogram and experiencing at least 1 epileptic seizure per month in the 3-month baseline period.
(3) The seizure types were consistent with the classification of seizures and epileptic syndromes by International League Against Epilepsy classifications in 1981 [9] and 1989 [10].

2.2. Visits

During the initial visit (V1), baseline demographics and disease characteristics were recorded as well as previous and current AEDs use. Seizure frequency during the past 3 months was recorded, retrospectively, including all seizure types occurring. A follow-up of one year was planned with visits after 3 (V2), 6 (V3), 9 (V4) and 12 months (V5) after baseline during which, type and frequency of the seizures, currently used drugs and doses, as well as side effects were documented. Body weight was assessed at start and final visit.

2.3. Treatment

Patients who had never taken any other anti-epileptic drugs before accepted monotherapy with levetiracetam and the ones who had taken other anti-epileptic drugs before included retained the former and added levetiracetam to accept combination therapy. Levetiracetam was started at a dose of approximately 10 mg/kg/day in two doses. The dose was titrated up with 10 mg/kg increments if seizures were poorly controlled but the maximum daily dose could not be more than 60 mg/kg/day.

2.4. Data management and statistical analysis

Data were checked for consistency and completeness and then entered into the database using double data entry. Evaluation was performed according to the intention-to-treat (ITT) principle.

Weekly seizure rates were calculated as a number of seizures between two consecutive visits divided by the length of the observation period (in days) multiplied by 7. Epileptic seizure frequency data were presented as changes (reductions) as well as response rates, where response was defined as an at least 50% (75% or 100%) reduction in seizure frequency.

The degree of side effects was defined as follows: "mild" if the side effects was not clinically obvious and lasted not longer than 2 weeks; "moderate" if it was obvious and lasted longer than 2 weeks but could not influence patients' normal daily life; "severe" if it obviously influenced patients' daily life or even needed therapy in hospital.

Descriptive statistical methods (i.e. frequency and summary statistics including arithmetic mean $\pm$ SD and median) were used. In addition, exploratory pre–post comparisons were performed using two-sided Wilcoxon's test for dependent samples. No adjustment for multiple testing was performed. Evaluation was performed with the program package SPSS version 13.0.

2.5. Ethics

An independent ethics committee was notified about the trial and gave approval. Patients provided informed consent to allow data verification between case report form and source data.

3. Results

In the study, a total of 129 patients were followed between June 1, 2007 and July 30, 2009. In 5 patients, data could not be validated because the presence of epileptic seizures turned out to be doubtful and in 4 patients, no follow-up data on efficacy was documented. As no adverse events (AEs) occurred in these patients, a total of 120 patients were included in the ITT efficacy analysis.

The mean observation period for these patients was 10.3 ± 3.5 months (range: 0.5–12 months).

3.1. Demographics and disease characteristics

Demographic and disease data are summarized in Table 1.The mean age was 4.5 ± 3.9 years (range: 0–16 years), 39.3% of the patients were female and the median duration of disease was 1.5 years.

Partial seizures occurred in 53(44.2%) patients and primary generalized occurred in 35(29.3%). Moreover, there were 20(16.7%) patients who suffered from infantile spasms and 9(7.5%) patients who suffered from Lennox–Gastaut syndrome. Most commonly reported seizure types were secondarily generalized tonic–clonic seizures (23.3%). Overall, the mean weekly seizure rate in the 3 months prior to the study was 67.4 ± 9.9 in the 120 evaluated patients.

Since the epilepsy diagnosis has been made, 22.5% of patients had been treated with one, 11.7% with two, 6.7% with three and 25.0% with more than three AEDs.

3.2. Anti-epileptic therapy

Totally, 37 patients (30.8%) accepted monotherapy and the other 83 patients (69.2%) accepted combination