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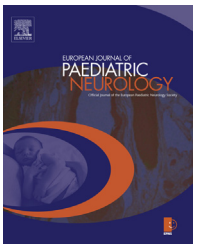

Original article

Intravenous levetiracetam in Thai children and adolescents with status epilepticus and acute repetitive seizures

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ABSTRACT

Background: Intravenous levetiracetam is an option for treatment of status epilepticus (SE) and acute repetitive seizures (ARS). However, there have been relatively few studies with children and adolescents. Also, an appropriate dosage has yet to be determined.

Aim: This study investigated the safety and the efficacy of levetiracetam for intravenous treatment of convulsive status epilepticus and acute repetitive seizures in children and adolescents.

Method: Retrospectively, the study reviewed the medical records of 19 male and 31 female patients under 18 years of age who had received intravenous levetiracetam treatment either for acute repetitive seizures or for convulsive status epilepticus. The patients were admitted between April 1st, 2010 and December 31st, 2011 to the Department of Pediatrics, Faculty of Medicine Ramathibodi Hospital, Mahidol University, Bangkok, Thailand. Data were collected on underlying illnesses, etiology of seizures, indication for levetiracetam therapy, initial dosage, rate of infusion, untoward effects during infusion and emerged complications. Efficacy of treatment was defined as the termination of seizure within 30 min of completing levetiracetam infusion and no seizure recurrence within 6 h of initial treatment.

Results: The age range of the 50 patients was from one day to 18 years (mean 79.6 months). The analysis included 52 episodes of 34 acute repetitive seizures (63.4%) and 18 convulsive status epilepticus (34.6%). Infusion rates ranged from 2 to 66 mg/kg/min (mean 29.6). Cessation of seizure was obtained in 59.6% of 52 episodes. Patients with underlying drug resistant epilepsy did not respond to levetiracetam therapy as well as patients with other etiology of seizures. There were no adverse drug reactions or untoward effects observed during the therapy.

Conclusion: Intravenous administration of levetiracetam is safe and effective for treatment of acute repetitive seizures and convulsive status epilepticus in children and adolescents.

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Failure of treatment may be related to underlying drug resistant epilepsy. Further study of appropriate initial dosage and pharmacokinetic variations in the patients is needed as possible explanation of the unresponsiveness.

1. Introduction

Levetiracetam is a broad-spectrum antiepileptic drug with proven efficacy as an adjunctive therapy for localization-related epilepsy in children, for juvenile myoclonic epilepsy in children and adolescents, and for primary generalized tonic-clonic seizures in adults. It has been recognized as a new generation antiepileptic drug with a favorable safety and tolerability profile, and insignificant drug–drug interaction.[1] Levetiracetam has been available in tablet form since 1999 and in oral solution since 2003. The United States Food and Drug Administration (US FDA) approved the intravenous formulation in July 2006.[1,2] Since then, levetiracetam has been used in the treatment of various types of seizures in children and adolescents. As of 2012 with the US FDA's approval, it has been used for drug-resistant focal-onset seizures.[3]

The availability of levetiracetam in the intravenous formulation provides a useful option when oral administration is temporarily unattainable in status epilepticus and acute repetitive seizures.[4] There have been many reports of its favorable efficacy in treatment of adult patients presenting with status epilepticus.[5–8] After being administered in the treatment of adult status epilepticus and acute repetitive seizures, its efficacy and safety for children were also reported and documented.[9–17] Recently, there have been reports on levetiracetam's role in the treatment of neonatal seizures with favorable outcomes.[18–23] However, the total number of patients in those studies was very small with a wide-range of initial dosage.

In Thailand, there are five intravenous antiepileptic drugs available. These are phenobarbital, phenytoin, fos-phenytoin, valproate and levetiracetam. Levetiracetam was included as an option for treatment of convulsive status epilepticus in the guidelines for epilepsy treatment by the Epilepsy Society of Thailand in 2011. Nevertheless, there have been very few reports in Thailand on these drugs' efficacy and safety, especially of levetiracetam. To date, there has been only one study that examined intravenous levetiracetam in 34 adult patients presenting with convulsive status epilepticus. The study reported a seizure-control rate of 61.8%.[24] This current study was therefore conducted to evaluate the efficacy and the safety of intravenous levetiracetam for treatment of convulsive status epilepticus and acute repetitive seizure in Thai children and adolescents.

2. Methods

A retrospective review was conducted of medical records of 50 patients under the age of 18 years admitted to the Department of Pediatrics, Ramathibodi Hospital, between April 1st, 2010 and December 31st, 2011. All of these patients received the intravenous levetiracetam for treatment of either acute repetitive seizures or convulsive status epilepticus. Acute repetitive seizure was defined as repeated seizures of which each lasted less than 5 min with recovery of consciousness between each seizure and that persisted for at least 30 min. Convulsive status epilepticus was defined as convulsive type of any single and prolonged tonic-clonic seizure that persisted for over 5 min and irrespective of whether any emergency medication administered.[10] The etiologies of seizures were classified according to the documented cause of seizures. The episode with definitive causes of seizures would be categorized into symptomatic group, while the episodes without definitive causes would be categorized into unknown group.

The study collected data on the underlying illnesses, etiology of seizures, indication for the use of levetiracetam, initial dosage, rate of infusion, and untoward effects during infusion and during the 24 h after administration. The efficacy of the treatment was categorized into 2 groups as respond-to-treatment and unresponsive. The group assignment was determined according to the cessation of seizures within 30 min after completion of infusion and no recurrence of seizures within 6 h after infusion. Patients with seizures that terminated within 30 min after levetiracetam infusion with no recurrence of seizure within 6 h were categorized as respond-to-treatment.

Descriptive statistical analyses were applied in this study. Demographic and clinical characteristics were analyzed with SPSS software version 21.0 (SPSS Inc., Chicago, Ill., USA). Student's *t*-test and chi-square analysis were applied for continuous variables and discrete variables, as appropriate. Fisher's exact test or chi-square test was employed for analysis of response to treatment according to sample size.

This study was approved by the Ethics Committee of the Human Right to Research Involving Human Subjects, Faculty of Medicine Ramathibodi Hospital, Mahidol University, document number MURA2013/561.

3. Results

Nineteen males and 31females were included in this study. Two patients had two separate admissions due to acute repetitive seizures or convulsive status epilepticus resulting in 52 total episodes for analysis. Patients' ages ranged from one day to 18 years (mean 79.6 months). The etiology of 52 episodes of acute repetitive seizures or status epilepticus consisted of 36 symptomatic etiology and 16 unknown etiology. The indication for administration of intravenous levetiracetam is shown in Table 1.

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