Brain & Development 38 (2016) 654–657

BRAIN & DEVELOPMENT
Official Journal of the Japanese Society of Child Neurology

www.elsevier.com/locate/braindev

Case Report

Aggravation of atonic seizures by rufinamide: A case report

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Received 27 November 2015; received in revised form 3 February 2016; accepted 8 February 2016

Abstract

Background: Rufinamide is a novel antiepileptic drug used as adjunctive therapy in patients with Lennox–Gastaut syndrome and provides seizure control especially in tonic and atonic seizures. Rufinamide is expected to be effective in intractable epilepsy when atonic and tonic seizures exist. However, rufinamide induced seizure aggravation has been reported in a few patients, which was not associated with a specific type of seizure.

Case: A 12-year-old boy with intractable epilepsy had tonic and atonic seizures despite treatment with valproic acid (3000 mg/day), levetiracetam (3000 mg/day) and clobazam (40 mg/day). Rufinamide was administered as adjuvant therapy. After 2 weeks on rufinamide, he experienced atonic seizure worsening, and the frequency of epileptic discharges increased. The deterioration in seizure frequency and epileptiform discharges resolved when rufinamide was discontinued.

Conclusion: Rufinamide may aggravate atonic seizures in patients with intractable epilepsy.

Keywords: Rufinamide; Intractable epilepsy; Atonic; Seizure

1. Introduction

Rufinamide is a novel antiepileptic drug that acts on voltage-gated sodium channels and is structurally different from the other antiepileptic drugs currently in use [1]. It was approved for adjunctive treatment of seizures associated with Lennox–Gastaut syndrome (LGS) in children over 4 years of age by the United States Food and Drug Administration. Efficacy of rufinamide has not yet been verified in patients with epilepsy except for LGS. Therefore, it is still considered as an orphan drug that was licensed only for LGS [2].

Rufinamide is considered to be effective in treating refractory epilepsy, especially when tonic and atonic seizures are present [3,4]. Although seizure aggravation by rufinamide has not been associated with any specific type of seizure, recent studies including an *in vitro* study have suggested that the worsening of seizure frequency may occur after the administration of rufinamide [1,2].

We hereby present the use of rufinamide as adjunctive therapy in a 12-year-old boy with intractable epilepsy. On the second week of rufinamide treatment, he developed atonic seizure aggravation, which was associated with worsening of epileptiform discharges. The frequency of seizures and epileptic discharges decreased soon after cessation of rufinamide.

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http://dx.doi.org/10.1016/j.braindev.2016.02.005

2. Case report

A 12-year-old boy with refractory seizures was referred to our pediatric neurology clinic. His prenatal and family histories were unremarkable. His developmental milestones were normal. At age 4.5 years he had a generalized tonic-clonic seizure that evolved into status epilepticus and multi-organ failure. He was monitored in the intensive care unit for 3 months. After discharge, his seizures remained uncontrolled despite using antiepileptic drugs including vigabatrin, levetiracetam, valproic acid, phenobarbital, clobazam and topiramate. His family did not consent to a ketogenic diet.

On admission, he had a few ictal periods per day characterized by eyelid blinking, tonic deviation of eyes and atonic seizures on valproic acid (3000 mg/day, trough serum level of valproic acid was 98 mg/L), levetiracetam (3000 mg/day) and clobazam (40 mg/day). His neurologic exam was unremarkable except for autism-like symptoms and mild mental retardation. Holter electrocardiogram, complete blood count, serum biochemistry and metabolic tests were normal. Magnetic resonance imaging of the brain revealed mild cortical atrophy. An electroencephalogram (EEG) with the international 10/20 system demonstrated normal background activity and fronto-temporal discharges [Fig. 1].

The patient's parents consented to the use of rufinamide as an off-label adjuvant therapy. Rufinamide was added to the baseline therapy at 100 mg/day and was titrated with an increment of 50 mg every 3 days up to 250 mg/day over 2 weeks. The seizure frequency remained the same during the first 2 weeks. He developed drop attacks up to ten times per day on fifteenth day of rufinamide treatment. His drop attacks, which lasted for a few seconds with sudden loss of muscle tone, were compatible with atonic seizures. Interictal EEG revealed excessive high amplitude epileptiform discharges in the fronto-central areas [Fig. 2]. The seizure frequency and epileptiform discharges decreased significantly after discontinuation of rufinamide [Fig. 3].

3. Discussion

We herein present a child with tonic and atonic seizures that were refractory to the antiepileptic drugs (vigabatrin, levetiracetam, valproic acid, phenobarbital, clobazam and topiramate). Rufinamide has been shown as an efficient antiepileptic drug to reduce seizure frequency in 50 percent of patients with intractable epilepsy, especially when tonic and atonic seizures exist [3]. Therefore, we preferred to use rufinamide as an adjuvant therapy to improve seizure control. However, the worsening of atonic seizure frequency occurred early after starting rufinamide treatment.

Seizure aggravation by rufinamide has been reported in 4–16% of patients with LGS [2,6]. Although studies reported a relation between rufinamide and increased seizure frequency, a specific seizure type linked to seizure aggravation has not been defined [6].

Rufinamide and carbamazepine, two drugs with different structures, act by influencing the fast inactivation of voltage-gated sodium channels [1]. Carbamazepine

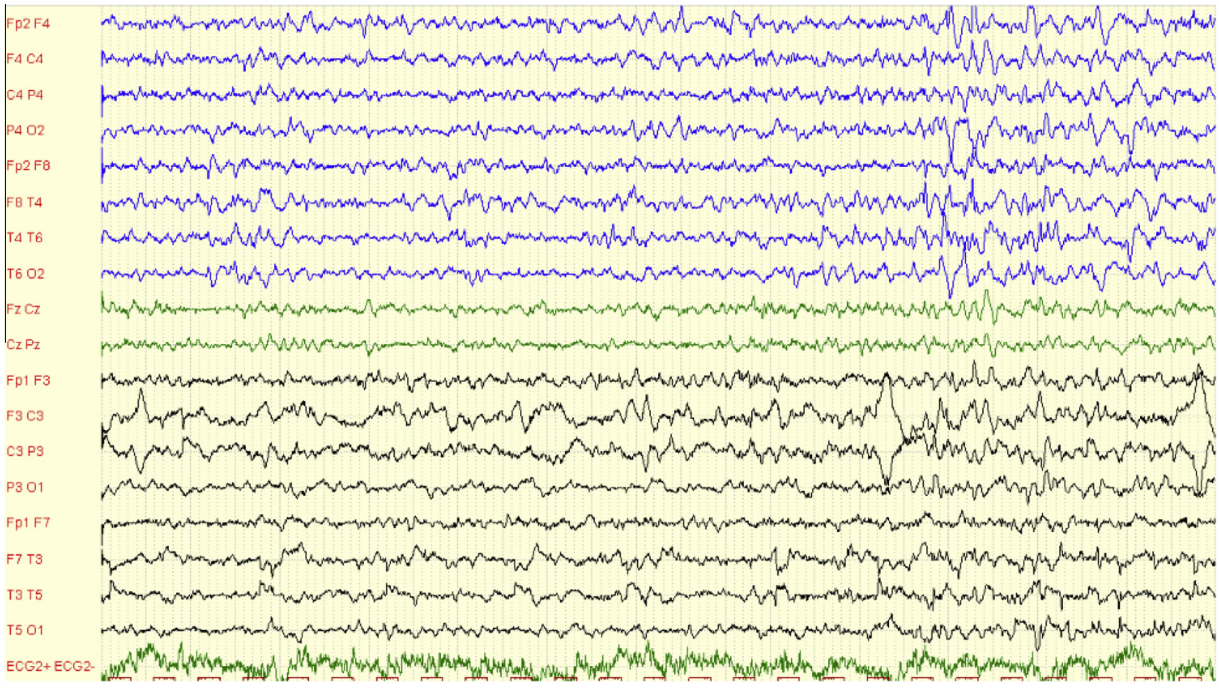

Fig. 1. Awake EEG before rufinamide treatment: the interictal EEG shows normal background activity with frontotemporal spikes.