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The efficacy and tolerability of Levetiracetam as an add-on therapy in patients with startle epilepsy

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Summary

Purpose: To evaluate the efficacy and tolerability of Levetiracetam as an add-on therapy in patients with startle epilepsy (StEp).
Methods: Ten (7 males and 3 females) were enrolled in the study. LEV was started at 500 mg bid, escalating over 1—2 weeks to maximal doses of 3000 mg daily, based on seizure control and tolerance for 13—28 months.
Results: The onset of startle seizures in patients with StEp varied from birth to 11 years. Six in 10 patients gave good responses to the treatment. There were adverse effects in three patients.
Conclusion: Many AEDs have been used by medically intractable patients with StEp for many years but the results were almost discouraging.

It was observed that 60% of the patients gave good response to LEV. Advanced studies are required to indicate the efficiency of LEV which proved to be effective on animals with audiogenic seizures on reflex epilepsies.

Introduction

Startle epilepsy (StEp) was first described in 1955.[1] It is mostly seen in patients with static or progressive encephalopathy in addition to comparatively fewer clinically normal cases.[2—5] Among the etiological causes are perinatal anoxia, stroke, Sturge—Weber syndrome, porencephalic cyst, postinflammatuar changes, dysplastic lesions, Down syndrome and familial neonatal convulsions. The insult typically occurs within the first 2 years of life and is often pre- or perinatal. The onset of StEp is in childhood or early adolescence. StEp is a well-defined clinical condition related to above-mentioned early lesions of the motor cortex. Neuroimaging findings can be normal, or it may show localized or diffuse lesions. The lateralized lesions usually involve sensorimotor

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and premotor cortex, and white matter. Focal or generalized atrophy is reported.[6] There are a few case reports or papers on groups of limited number of patients with StEp. The treatment of StEp is not always successful because total control of seizures is nearly impossible. The prognosis is usually bad especially in patients with preexisting severe encephalopathies. Because of the scarcity of patients with StEp, drug trials involving only a few patients could be done.[2,3,7]

Levetiracetam (LEV) is well tolerated with favorable pharmacokinetic profile that includes minimal protein binding, lack of hepatic metabolism and twice a day dosing.[8–12]

In this study our aim is to evaluate prospectively the efficacy and tolerability of LEV as an add-on therapy in patients with StEp.

Patients and methods

Out of 7759 patients, thirty with seizures triggered by unexpected stimulus have been diagnosed as StEp in Epilepsy Outpatient Clinic of Neurology Department since 1979. Only thirteen of 30 patients could be followed since only they came for their controls regularly while the others showed up either rarely or never for their follow-ups. The patients' files are reviewed with respect to their personal history, the onset of seizures (startle and spontaneous), frequency of seizures, provoking factors, neurological examination, mental retardation, neuroradiological findings, previously and currently used antiepileptic drugs (AEDs), responses of their spontaneous and startle seizures to LEV. Only 3 of 13 patients had good control seizure, i.e. they had no more startle seizures but only a few spontaneous seizures. They had no differences from the patients with intractable startle epilepsy in terms of the above-mentioned risk factors. The seizures of the other 10 patients were difficult to control despite the regular use of adequate AEDs. To test IQ, Alexander, Good enough and Cattell IQ tests are preferred to Wechsler Adult Intelligence Scale (WAIS) test since the latter has not been standardized for Turkish population. All patients were tested with only 1 of the three tests when applicable.

Their seizure diaries had been kept either by themselves or their families for 2 months before LEV treatment. They were included in the study to receive LEV treatment as an add-on therapy. LEV was started at 500 mg bid, escalating over 1–2 weeks to maximal doses of 3000 mg daily, based on seizure control and tolerance for 13–28 months. Patients had used upto 7 types of AEDs separately and during the study they used 1 to 3 types of AEDs simultaneously in addition to LEV. The dosage was adjusted individually for each patient with startle epilepsy. Visits were planned to be every 4 weeks, by alternating visits to hospital or calling the patient from home.

All patients and/or their parents gave written informed consent to the study which was done without both any specific funding and the involvement of any pharmaceutical company.

Results

There are 7 males and 3 females in our study group. The mean age of the patients is 26.93 ± 3.87 (21–34). In their previous history of the patients, birth hypoxia in 4, head trauma in 2, meningitis in 1, perinatal stroke in 1, prolonged birth and small gestational age in 1, subdural and intraventricular hematoma in 1, febrile or nonfebrile convulsion in 2 were found. Febrile and nonfebrile convulsions did not recur until the onset age of seizures. They had no previous histories of status epilepticus.

The onset of startle seizures in patients with StEp varied from birth to 11 years. The mean onset of age of epilepsy was 5.0 ± 4.71 years and the mean duration of epilepsy was 21.9 ± 5.82 years. The patients had two types of seizures, startle and spontaneous; both with the same characteristics: 7 patients had tonic seizures, 5 of whose were asymmetrical tonic. One patient had left focal motor seizures and 2 had partial and/or secondary generalized seizures in addition to their startle seizures. The main triggering stimuli for their startle seizures were sudden sound, found in all the patients, followed by touching or hitting any part of their bodies. The stimuli were sudden sounds in 10 patients, touching and sound in 7, stumbling in 2, fear, pain, excitement or scary dreams in 3 (Table 1). Both startle and spontaneous seizures were seen in patients with StEp while spontaneous ones were rare.

Abnormality was found in 9 patients in their neurological examination, the most common findings being hemiparesis with hyperactive reflexes and an extensor plantar response in 50%.

Due to the diverse features of the patients, different IQ tests were performed for each. The mentally retarded and borderline IQ patients constituted 70% of the group.

4 of the patients were mentally retarded, (3 (30%) severe, 1 (10%) moderate) and 3 (30%) had borderline IQ. It was not required to measure the IQ of 2 patients who were clinically normal.

Magnetic resonance imaging (MRI) showed abnormality in 8 patients. The abnormal MRI findings