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USE OF LEVETIRACETAM IN STRUCTURAL BRAIN LESIONS ASSOCIATED WITH REFRACTORY SEIZURES

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ABSTRACT

BACKGROUND. Approximately 40% of all individuals with epilepsy have medically refractory or intractable seizures. Among the most common etiologies are Mesiotemporal and tuberous sclerosis, Sturge-Weber syndrome, cerebral tumors, arteriovenous malformations, developmental malformations, and sequel of cerebral infections, infarcts or trauma. Levetiracetam (LEV) is a second generation AED, indicated as adjunctive therapy in adults with partial seizures. OBJECTIVE. To assess the efficacy and safety of LEV add-on therapy in patients with structural brain lesions associated with medically refractory partial epilepsy. MATERIAL AND METHODS. Twelve patients (5 M and 7 F; aged 41.6 ±7.6 years) with tumor and non-neoplastic brain lesions associated with refractory seizures were included in the study. Diagnosis was based on the criteria of ILAE. All patients had an adjunctive therapy with LEV (1000-3000 mg/daily) for at least six months. Drug efficacy was assessed as change in seizure frequency. Safety was assessed as measurement of retention rate and reporting the drug related adverse effects. Neuroimaging, EEG, and clinical follow-up were performed before and after initiation of LEV add-on therapy. RESULTS. LEV add-on therapy reduced seizure frequency in 85 percent of patients and 46 percent became seizure free. Retention rate was 100 percent for patients treated with LEV. The most common side effect was transient somnolence, noted in 25 percent of patients. CONCLUSION. This study confirms the efficacy and safety of LEV as add-on therapy in patients with structural brain lesions. Due to its unique mechanisms of action, LEV presents a new therapeutic challenge even for patients with highly refractory partial epilepsy.

Key words: Levetiracetam, structural brain lesions, refractory seizures

INTRODUCTION

Mesiotemporal sclerosis, tuberous sclerosis, Sturge-Weber syndrome, cerebral tumors, hamartoma, arteriovenous malformations, developmental malformations, and sequel of cerebral infections, infarcts or trauma are the most common etiologies that cause refractory seizures (1,5,7,9,12). The most frequently prescribed anticonvulsants often interact with other medications, complicating their dosing and diminishing their effectiveness (7,8,13,15). Recently, significant advances in epileptology are related to the development of new antiepileptic drugs (AEDs), as well as better understanding of their mechanisms of action and drug interactions (5,7,8,12,15). Levetiracetam (LEV) is a second generation AED, indicated as adjunctive therapy in adults with partial seizures (1,2,4,6,9,10,12,14). Because of its unique mechanism of action (specifically reduces the N-type high-voltage-activated Ca2+ current and opposes the action of negative modulators of GABA and glycine receptors), it has been postulated that LEV may be effective in controlling brain lesion-induced refractory seizures (1,2,3,11,14,15,16).

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OBJECTIVE

To assess the efficacy and safety of LEV add-on therapy in patients with structural brain lesions associated with medically refractory partial seizures.

MATERIAL AND METHODS

Twelve patients (5 males and 7 females; aged 41.6 ±7.6years) with structural brain lesions associated with refractory partial seizures were included in the study. Five (5) patients had brain tumors, 3 low-grade astrocytomas (Case 1) and 2 meningiomas. Seven (7) had non-neoplastic brain lesions - 3 benign arachnoid cysts (Case 2), 2 cerebral angiomas (Case 3), and 2 cerebral trauma with sequel (Case 4). They presented either with simple (70 percent) or with complex partial (30 percent) seizures. Diagnosis was based on the criteria of ILAE. All patients had an ad-

junctive therapy with LEV (1000-2000 mg/daily) for at least six months. Drug efficacy was assessed as change in seizure frequency (percentage of patients who became seizure free and percentage of patients who responded with >50% reduction in seizures). Safety was assessed as measurement of retention rate (percentage of patients continuing the treatment) and reporting the drug related adverse effects. Neuroimaging, EEG, and clinical follow-up were performed before and after initiation of LEV add-on therapy.

CASE 1. A 56-years old female with low-grade glioma who experienced increased simple partial seizures activity after surgery was admitted to the clinic. EEG findings showed left frontotemporal focus of epileptic activity. Postoperative CT scans demonstrated a residual hypodense lesion and lack of tumor recurrence (Fig.1).

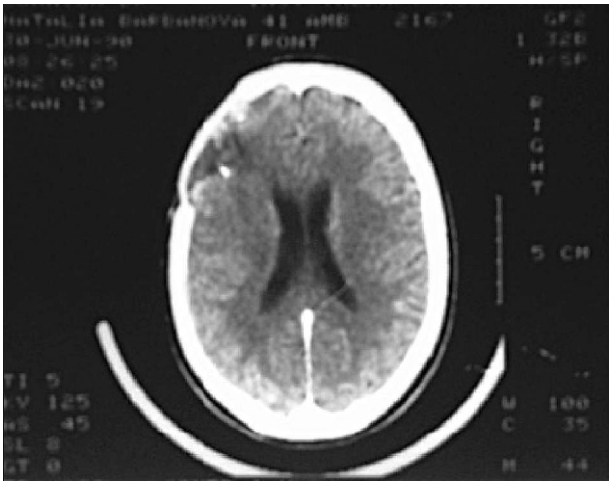

Fig. 1.

CASE 2. A 55-years old male was admitted to the clinic with medically refractory simple partial seizures.

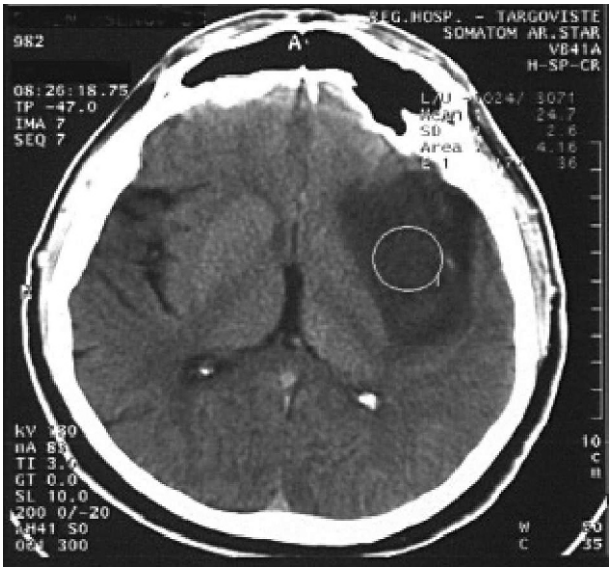

Fig. 2.

EEG demonstrated epileptic focus in the left frontotemporal region. CT scan showed a well-defined, non-enhancing hypodense lesion in the left frontotemporal region (Fig.2).

CASE 3. A 25-years young male with SWS was admitted to the clinic with increased frequency of secondarily generalized partial seizures. EEG revealed a focus of epileptic activity in the left temporal region. CT scans showed bilateral contrast enhancing hyperdense lesions in the temporal and occipital regions (Fig. 3).

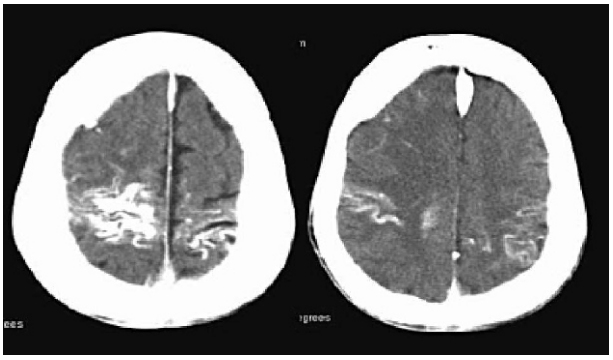

Fig. 3.

CASE 4. A 17-years young male with fire-caused brain injury was admitted to the clinic with increased frequency of complex partial seizures 3 years after surgery. EEG revealed epileptic activity in both temporal regions. Postoperative CT scans showed a residual hypodense lesion with residual projectiles in the right frontal region (Fig. 4).

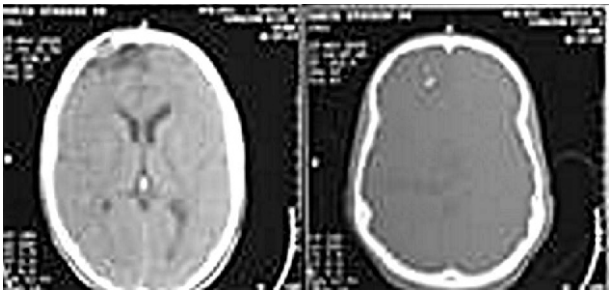

Fig. 4.

RESULTS

LEV add-on therapy reduced seizure frequency in 85 percent of patients. Over the treatment period 46 percent of patients became seizure free. Drug efficacy was higher in individuals with non-neoplastic brain lesions. Retention rate was 100 percent for patients treated with LEV. The most common side effect was transient somnolence, noted in 25 percent of patients.

DISCUSSION

Approximately 40% of all individuals with epilepsy have medically refractory seizures (failure of two or more drugs and occurrence of one or more seizures per month over 18 months) that continue to occur despite treatment (5,13,16). These acquired intractable seizures are most common in patients with brain malignancies and non-neoplastic cerebral abnormalities (4,7,8,11,14,15). They often impact on patients' quality of life and survival. Clinical trials and studies are suggestive that better understanding of underlying processes and biological mechanisms guarantees the successful treatment (5,8,10,12). Furthermore, evidence exists that all of the new AEDs demonstrate efficacy as add-on therapy in patients with refractory seizures (5,8,13,15). Accordingly, Report of the American Academy of Neurology and the American Epilepsy Society recommends using LEV (Level A) in symptomatic epilepsy associated with suspected or known structural brain lesions (7). Respectively, we studied a group of patients with primary brain tumors or non-neoplastic lesions and uncontrolled seizures. Our results supported the previously reported findings that LEV add-on therapy reduces seizure frequency in most patients, with nearly 60 percent becoming seizure free over the treatment period (2,3,6,9,10,16). In correspondence with many observations, somnolence was the most common side effect noted in our patients (1,2,4,14,15).
Review of the literature reveals that multifactorial mechanism of epilepsy is considered in patients with different structural brain lesions (2,5,8,9,12,16). Based on our own clinical, neuroimaging, and electrophysiological notices, we suppose that the most likely are cerebral edema and ischemia, local metabolic imbalances, changes in neuronal and glial enzyme expression, and altered immunological activity.

CONCLUSION

In summary, the new antiepileptic drug LEV is indicated as adjunctive therapy in the treatment of partial seizures in adults. Accordingly, this study confirms its efficacy and safety as add-on therapy in patients with structural brain lesions. We suggest that, due to the unique mechanisms of action, LEV presents a new therapeutic challenge even for patients with highly refractory partial epilepsy.

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