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NOVEL PHARMACOTHERAPY IN REFRACTORY EPILEPSY ASSOCIATED WITH STRUCTURAL BRAIN LESIONS

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ABSTRACT

BACKGROUND: Patients with various structural brain lesions often suffer from seizures. Refractory epilepsy is the most common in brain tumors, vascular malformations, and sequel of cerebral infections, infarcts or trauma. OBJECTIVE: To evaluate the efficacy and safety of new AEDs in patients with medically refractory seizures associated with structural brain lesions. MATERIAL AND METHODS: Twenty-six (26) patients (8 M; 18 F), aged 48.4± 7.6 years, with simple (65%) or complex partial (35%) seizures associated with cerebral tumors (12 p) and non-neoplastic brain lesions (14 p) were included in the study. Diagnosis was based on the criteria of ILAE. Patients were treated with OXC (10 cases), LTG (9 cases), and LEV (7 cases) for at least six months. Efficacy and tolerability were assessed on the basis of changes in seizure frequency and reporting the drugs side effects. Structural neuroimaging, EEG, and clinical follow-up were performed before and after AEDs addition. RESULTS: Eighteen (18) patients (72%) were seizure-free after six to twenty-four months treatment period and 8 (28%) experienced some rare partial seizures but no more generalized attacks. Side effect of mild somnolence was observed in 4 patients treated with LTG during the first 3 weeks of the treatment, of transient dizziness in 3 patients under OXC, and transient fatigue in 2 patients treated with LEV. CONCLUSION: In accordance with our own findings and literature review, we suggest that new AEDs due to their efficacy and good safety profile might be useful for the epilepsy control in patients with medically refractory seizures associated with structural brain lesions.

Key words: refractory epilepsy, novel pharmacotherapy, efficacy, side effects

INTRODUCTION

Epilepsy is the most common neurological disorder, estimated to affect 50 million people worldwide (12). Patients with various structural brain lesions (tumors, vascular malformations, and sequel of cerebral infections, infarcts or trauma) often suffer from seizures (1,2,4,5,7,13). Refractory epilepsy is common in these cases and a role for multidrug resistance proteins has been suggested (4,9,10,12).

The most frequently prescribed "first-generation" anti-epileptic drugs (AEDs) interact with other medications, complicating their dosing and effectiveness (2,9,12). Many second-generation AEDs are not metabolized in the liver and have fewer drug interactions (5,6,8,11). This must be considered when designing a treatment strategy for refractory epilepsy and evaluating efficacy, tolerability, and toxicity (1,2,8,12). The introduction of new AEDs in the last twenty years has provided greater choice for patients and physicians (3,6,8,9,10,11,13). Accordingly we decided to evaluate the efficacy and safety of Oxcarbazepine (OXC), Lamotrigine (LTG), and Levetiracetam (LEV) in patients with medically refractory partial and secondary generalized seizures associated with different structural brain lesions.

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MATERIAL AND METHODS

Twenty-six patients (26) (8 M; 18 F), aged 48.4 ±7.6 years, with uncontrolled seizures associated with cerebral tumors (12 p) and non-neoplastic brain lesions (14 p: benign arachnoid cysts - 4 p, brain infarction with sequel - 4 p, ce-

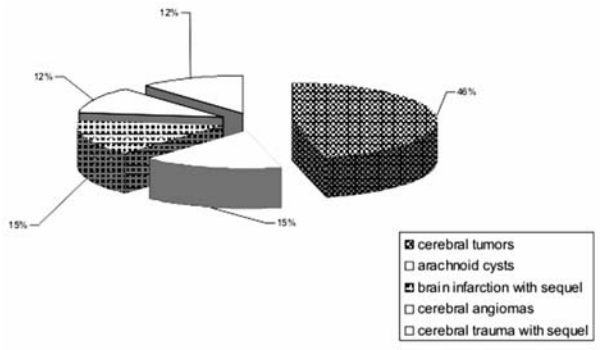

Fig.1. Distribution of patients according to the type of brain lesion.

rebral angiomas - 3 p, and cerebral trauma with sequel - 3 p) were included in the study (Fig. 1). Patients presented with simple (65%) or complex partial (35%) seizures with secondary generalization. Diagnosis was based on the criteria of International League Against Epilepsy (ILAE). Ten patients were treated with OXC (1200-1800 mg/daily), nine with LTG (200-400 mg/daily), and seven with LEV (2000-3000 mg/daily) for at least six months (Fig. 2).

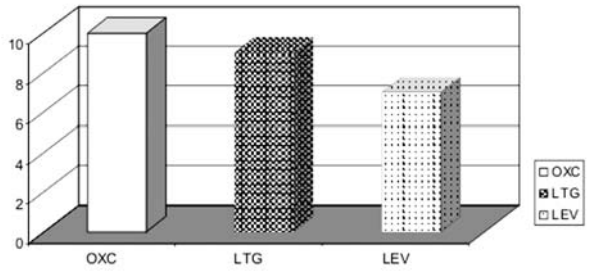

Fig. 2. Distribution of patients according to the AEDs.

Efficacy was assessed on the basis of changes in seizure frequency and tolerability with reporting the adverse effects related to the drug. All patients underwent computed tomography (CT) or magnetic resonance imaging (MRI), electroencephalography (EEG) monitoring, and clinical assessment before and every six months after AEDs addition.

RESULTS

Efficacy

All patients exhibited clinical improvement. Eighteen (18) patients (72%) were seizure-free after 6 to 24 months treatment period and 8 (28%) experienced some rare partial seizures but no more generalized attacks.

Adverse Events

Side effect of mild somnolence was observed in 4 patients treated with LTG during the first three weeks of the treatment, of transient dizziness in 3 patients under OXC, and transient fatigue in 2 patients treated with LEV.

DISCUSSION

According to the Consensus proposal by the ad hoc Task Force of the ILAE Commission on Therapeutic Strategies, about 40% of patients have structural/metabolic etiology of epilepsy (1). Most of them are considered drug resistant, because the application of 2 AEDs as a mono- or combined therapy is not successful (2,5,7,12). Although the significant success achieved in the treatment of epilepsy over the past decades, about one third of patients with epilepsy have bad seizures control with current AEDs (5,10,12,13). Clinical evidences exist that even in patients with efficacious pharmacotherapy; the underlying mechanisms of epileptogenesis are not successfully affected (4,7,9).

In relation to these data our study group consisted of patients with acquired or congenital structural brain lesions. All patients had intractable seizures requiring add-on therapy with new AEDs. The analysis of our results revealed that use of OXC, LTG, and LEV reduced significantly the frequency of seizures in all patients (3,6,8,10,11). These findings are in accordance with recent studies confirming the high efficacy of novel anticonvulsants (5,6,10,12). In addition, the percentage of side effects observed in our study groups (respectively 30.0%, 44.4%, and 28.5%) is consistent with literature data (4,6,9,11). Furthermore, the most common side effects we found in our patients treated with OXC (mild transient dizziness), LTG (transient somnolence), and LEV (fatigue) are similar to those described in the available literature (1,3,6,8,11).

In summary, despite the heterogeneous and limited group of patients included in this study, our observations revealed data that proved the use of new AEDs in successful managing of refractory epilepsy.

CONCLUSION

In accordance with our own findings and literature review, we suggest that new AEDs such as LTG, OXC, and LEV demonstrate high efficacy and good safety profile. Obviously, this novel pharmacotherapy benefits the epilepsy control and improves the quality of life of patients with medically refractory seizures associated with structural brain lesions.

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