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Add-on topiramate in the treatment of refractory partial-onset epilepsy: Clinical experience of outpatient epilepsy clinics from 11 general hospitals

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Summary An open, prospective, observational study was performed to assess efficacy and adverse-event profile of topiramate as add-on therapy in epilepsy. Outpatient neurology clinics from 11 general hospitals in Greece participated in the study. In total, 211 patients with treatment resistant partial-onset seizures who met the inclusion criteria, were studied. After baseline evaluation, topiramate was given at a target dose of 200 mg/day over a 1-month titration period. In the subsequent maintenance period, the topiramate dose could be varied according to the clinical results. Patients were followed for in total 6 months, with monthly visits and regular physical, neurological and laboratory examinations. Seizure frequencies

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decreased to 35—40% of baseline values following 3 months of treatment and remained relatively constant thereafter. The average monthly seizure frequency over the 6-month study period was 4.61, compared to 9.21 at baseline. The number of responders (patients with at least 50% reduction in seizure frequency) followed a similar pattern, i.e., increase during the first 3 months levelling off at a final 80—85% response rate. Of those completing the study, 30% had been seizure-free for at least 3 months and 12% for 5 months. Topiramate was well tolerated, no deviations in laboratory values were found. Adverse events appeared to occur less frequently, and antiepileptic effects were more pronounced in this prospective open-label study than in earlier reports from randomised controlled trials. The nature of the patient population and the application of individualised dose optimisation are proposed as contributing factors to explain the favourable results of this study.

Introduction

Monotherapy with one antiepileptic drug (AED), and even combination therapy with two or more AEDs together, quite often fail to produce adequate seizure relief in patients with epilepsy. New AEDs have become available over the past decade, providing new treatment options, and topiramate appears to be one of the promising examples. Topiramate is authorised for the adjuvant treatment of partial onset seizures with or without secondary generalisation, primary generalised tonic—clonic seizures and seizures associated with Lennox—Gastaut syndrome. In comparison with other AEDs, it ranks among the most efficacious as was shown in a meta-analysis.[1] The number of patients to be treated, in order to obtain at least 50% reduction in seizure frequency, was between six and nine for other new AEDs such as tiagabine, zonisamide, lamotrigine and gabapentin, but was only three for topiramate.[2] Randomised placebo-controlled studies[3,4] showed that the topiramate dose required to produce these effects, was in the range of 200—400 mg/day. In recent studies, topiramate was also found efficacious as monotherapy.[5,6] A double-blind randomised trial comparing topiramate (100 or 200 mg/day) with either carbamazepine or valproate, showed that topiramate was as effective as these older AEDs.[7] Consequently topiramate received official approval for use as monotherapy in most European countries.

Regarding everyday clinical practice, it is good to keep in mind that published data on topiramate add-on treatments were almost exclusively gathered in randomised controlled studies. Such studies applied fixed doses and predetermined treatment regimens that are assigned to patients on the basis of a randomisation schedule rather than taking the patient's personal needs into account.[3,8—12] Clinical practice on the other hand, focuses on the individual patient and aims at optimising his or her personal therapy. Considerable differences in drug susceptibility are known to exist from patient to patient, and pragmatic titration is the usual approach to determine which dose balances best antiepileptic efficacy and adverse event profile in a particular case.

We decided to investigate the everyday use of topiramate in adult epilepsy patients with therapy-resistant partial onset seizures, selected as outpatients of non-specialised neurology clinics of general hospitals.

Patients and methods

Patients

Male and female patients, 18 years of age and over, were eligible if they had experienced at least four partial-onset seizures with or without secondary generalisation, according to the International Classification of Seizures,[13] in the 2 months preceding study entry. Patients had to be treated with one or more AEDs during the immediate pre-trial period. Female patients of childbearing potential had to use acceptable contraceptive methods during the trial; pregnant or breast-feeding women could not be included. Patients were excluded if they had a treatable cause of seizures, progressive neurological disorder, or a history of generalised status epilepticus in the past 3 months. Patients with a medical or social state that would influence their reliable participation, or who were unable to complete the diary or take their medication (not even with available help), were also excluded.

The study was conducted in accordance with the principles of the Declaration of Helsinki. After approval by the applicable Institutional Review Board, written informed consent was obtained from each patient prior to study entry or any study-related procedures.