DRUG TREATMENT

Efficacy and tolerability of topiramate as first line add-on therapy of epilepsy

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Objective: The purpose of this ongoing prospective study is to evaluate the use of topiramate (TPM) as first line add-on therapy, i.e. after a first antiepileptic drug (AED) has failed due to lack of efficacy, lack of tolerability or both.

Methods: This is an interim analysis of a prospective open-label multicenter observational study. Patients with epilepsy ≥ 12 years of age who were unsuccessfully treated with one previous antiepileptic drug (AED) due to lack of efficacy and/or tolerability were eligible for enrollment. Patients were evaluated at baseline and after 6, 16 and 30 weeks. Doses of TPM and the previous AED could be adjusted individually. Seizure frequency and adverse events were assessed at each visit.

Results: Fifty-two patients (48% male, mean age 45 ± 15 years) were enrolled. Sixty-seven percent had partial epilepsy, 29% had generalized epilepsy, 4% were unclassified. Median observation period was 30.9 weeks. Patients were switched mainly from carbamazepine (58%) valproic acid (25%), or phenytoin (19%). Reasons for initiating TPM were lack of efficacy (92%) and lack of tolerability (10%) of the previous AED. At endpoint, the median dose of TPM was 125 mg/day. 47% of the patients received - 100 mg TPM/day and 41% between 100 and 200 mg TPM/day at the end of the observation period. In 35 % of the patients the baseline AED could be permanently discontinued.

Mean seizure frequency decreased from 8.4/month to 1.8/month ($p<0.001$ vs. baseline). Fifty-one percent of the patients remained seizure-free throughout the study. Nine out of 52 patients (17%) had an adverse event. Nausea was the only adverse event which was reported more than once (n=3). Except for one patient with memory difficulties, no cognitive adverse events were reported. Overall, 84 % of the patients continued treatment with topiramate after the end of the 30-week study period.

Conclusion: Topiramate was effective and well tolerated as first line add-on AED in the treatment of partial and generalized epilepsy. Tolerability was very good, most likely due to TPM doses used in a range of 100 – 200 mg/day. In addition, early reduction or discontinuation of the previous AED most likely contributed to fewer CNS-related side effects. Based on these results and recent encouraging monotherapy data[1,2], topiramate is a good therapeutic option for an alternative monotherapy.

References

1. Gilliam FG, Veloso F, Bomhof MA, *et al*. A dose-comparison trial of topiramate as monotherapy in recently diagnosed partial epilepsy. *Neurology* 2003; 60: 196-202.
2. Privitera MD, Brodie MJ, Mattson RH, Chadwick DW, Neto W, Wang S. Topiramate, carbamazepine and valproate monotherapy: double-blind comparison in newly diagnosed epilepsy. *Acta Neurol Scand* 2003; 107: 165-75.