EPILEPSY

Topiramate for infants with refractory partial seizures

Adjunctive topiramate does not substantially reduce the rate of seizures in infant with refractory partial-onset seizures, Novotny *et al.* report. "These results imply that the development of new therapies targeted to the underlying neurobiology of epilepsy in infants is required," comments Edward Novotny, of the Seattle Children's Hospital, University of Washington, USA.

Despite the fact that the incidence of seizures and epilepsy is at its greatest in infancy, very few rigorous, prospective clinical investigations of the safety and efficacy of medications for this age group have been carried out. Prospective studies in older children and adults have demonstrated that topiramate is an effective and well-tolerated antiepileptic agent. For these reasons, Novotny's group designed a prospective, placebo-controlled, double-blind study to assess the efficacy, safety, and tolerability of adjunctive topiramate in infants with refractory partial-onset seizures.

130 infants aged 1–24 months (mean age 12 months) received either daily topiramate in doses of 5 mg/kg, 15 mg/kg or 25 mg/kg, or placebo for 20 days, in addition to their existing regimen of antiepileptic drugs.

"Topiramate was not effective as adjunctive treatment in this study of 130 infants with refractory partial onset seizures," Novotny comments. The median percentage reductions in daily partial-onset seizure rate from baseline to final assessment did not differ significantly between the 25 mg/kg topiramate group and the placebo group (20.4% versus 13.1%, $P = 0.97$); the lower doses of topiramate were also not significantly different from placebo. Although no evidence of class I efficacy was shown, no unforeseen safety concerns associated with topiramate in this patient group were observed.

The investigators suggest that refractory partial-onset seizures in infants are fundamentally different to those in older children and adults, which could explain the conflicting results observed in topiramate therapy studies. Novotny adds that the negative outcome may also be related to the treatment duration during the study, which was short compared with trials in adults.

"The study demonstrates that innovative approaches to the design of clinical trials in this age group are needed," Novotny concludes. His research group plan to analyze an open-label portion of the study for both efficacy and safety in this population.

Lisa Richards

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