EFFECTS OF TOPIRAMATE ON LANGUAGE FUNCTIONS

Investigators at Chonbuk National University Medical School, Korea, report the effects of topiramate on language functions in 38 newly diagnosed epileptic patients, mean age 10 +/- 2 years and 8 months. The epilepsy was complex partial in 34, including BECTS in 5, simple partial in 2, and idiopathic generalized in 2. MRIs showed no significant abnormality. A test of language problem solving abilities (TOPS) showed worsening of all parameters during treatment with topiramate monotherapy, with shortened mean length of utterance in words during response, ambiguous answers, difficulty in selecting appropriate words, more time to provide answers, and incorrect grammar. A Korean version of the Peabody Picture Vocabulary Test of receptive vocabulary development showed an increase in receptive vocabulary development in 73.7% patients after topiramate, whereas 26.3% showed a decrease. Language tests should be considered in children during treatment with topiramate. (Kim SJ, Kim MY, Choi YM, Song MK. Effects of topiramate on language functions in newly diagnosed pediatric epileptic patients. **Pediatr Neurol** 2014 Sep;51(3):324-9).

COMMENTARY. Topiramate may cause linguistic problems in patients treated for epilepsy or migraine. A functional MRI study of language disturbances in subjects with migraine headache during treatment with topiramate demonstrated reduction in migraine frequency associated with a "remapping" of the language cerebral network. The main fMRI measure was pattern activation of prefrontal regions (Brodmann's areas 44, 45, and 46) in both left and right hemispheres. Changes in brain activity were observed during the phonemic task in patients with language disturbances [1]. In children with partial epilepsies treated with topiramate, answers to questions become more ambiguous, phrased in shorter sentences, and have a delayed response because of difficulties in word choice selection.

References.

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QUINIDINE IN TREATMENT OF MIGRATING PARTIAL SEIZURES OF INFANCY

Investigators at Children's Hospital of Philadelphia, PA, report a 3-year-old female who had presented with seizures at 10 weeks of life. Seizures were characterized by brief episodes of eye deviation, lip smacking, and alternating unilateral motor activity. EEG showed focal sharp and slow waves in runs that migrate between left and right hemispheres and evolve into near-continuous seizures. Neurological and general physical examinations and brain MRI were normal. Whole exome sequencing demonstrated a heterozygous missense mutation in KCNT1, a mutation previously described in 3 patients with migrating partial seizures of infancy (MPSI). Trials of multiple conventional AEDs were without benefit, the ketogenic diet partially controlled seizures but was associated with regression of development, and a trial of quinidine was considered justified. After 1 week following the addition of quinidine to the AED polytherapy and ketogenic diet, seizures ceased and she was seizure-free for 6 weeks. Developmentally, head control

improved and she spoke her first words. At the last follow-up, she had been seizure-free for >4 months, without adverse events. This case illustrates a novel approach to seizure treatment using a rapid identification of genetic mutation (in KCNT1) that can lead to targeted treatments (quinidine acts as a pore blocker, normalizing pathological potassium conductance in mutant KCNT1 channels). (Bearden D, Strong A, Ehnot J, DiGiovine M, Dlugos D, Goldberg EM. Targeted treatment of migrating partial seizures of infancy with quinidine. **Ann Neurol** 2014 Sep;76(3):457-61).

COMMENTARY. MPSI is an early onset epileptic encephalopathy characterized by randomly migrating focal seizures and psychomotor deterioration. Death, usually from intractable seizures or respiratory complications, often occurs within the first years of life [1]. MPSI is associated with mutations in a variety of genes, most commonly KCNT1, a known target of some cardiac drugs, including quinidine. The authors caution that quinidine exhibits drug interactions, inhibiting the metabolism of many antiepileptic medications. QT prolongation is a common adverse effect, necessitating close EKG monitoring.

References.

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DEMYELINATING DISORDERS

COGNITIVE OUTCOME OF CHILDHOOD-ONSET MULTIPLE SCLEROSIS PATIENTS

Investigators on behalf of the MS Study Group of the Italian Neurological Society performed a third cognitive assessment on 48 of 63 patients with childhood or juvenile MS in the original cohort and compared with 46 healthy controls. At year 5, 38% of the subjects with MS had cognitive impairment (defined as the failure of =/>3 tests). Between years 2 and 5, 66.7% of patients showed improvement on the individual cognitive impairment index. However, comparing baseline and 5-year testing, cognitive impairment index deterioration occurred in 56% of the patients, improvement in 25%, and stability in 18.8%. Deteriorating performance was related to male sex, younger age and age at MS onset, and lower education. On multivariate analysis, none of these variables was demonstrated. Systematic neuropsychological screening is recommended in this population of pediatric–onset MS patients showing a heterogeneous cognitive outcome. (Amato MP, Goretti B, Ghezzi A, et al. Neuropsychological features in childhood and juvenile multiple sclerosis. **Neurology** 2014 Oct;83(16):1432-8).

COMMENTARY. Pediatric-onset MS (POMS) represents 3% to 5% of the whole MS population, and one third of the POMS population has cognitive impairment. MS-related cognitive problems are attributed to their occurrence during periods of brain growth, myelination, and neural-network maturation [1]. MRI studies show reduced brain volume, and reduced thalamic volume and reduced corpus callosal area can distinguish children with cognitive impairment from those with intact cognitive performance [2][3].