OXCARBAZEPINE ADJUNCTIVE THERAPY FOR PARTIAL SEIZURES

The safety and efficacy of oxcarbazepine (OXC) as adjunctive therapy for refractory partial seizures were evaluated in 267 patients in a multicenter (47 centers in 8 countries; Argentina, Chile, Uruguay, Australia, New Zealand, Canada, Israel, and the USA), randomized, placebo-controlled trial, and reported from the Children's Hospital, Cincinnati, OH. Children, aged 3 to 17 years, with inadequately controlled seizures and taking one or two concomitant antiepileptic drugs, received either OXC 6 to 51 mg/kg/day (median, 31 mg/kg/d) orally or a placebo, in a 112-day double-blind treatment phase.

The median percent reduction from baseline seizure frequency (56-day preliminary observation period) was 35% versus 9% for OXC and placebo groups, respectively (p=0.0001). The percent of patients with a >50% reduction in seizure frequency per 28 days was 41% for the OXC group and 22% with placebo (p=0.0005). Adverse events were reported in 91% and 82% of the OXC and placebo groups, respectively. A twofold or greater incidence of vomiting, somnolence, dizziness, and nausea occurred in children treated with OXC. Fourteen patients (10%) in the OXC group and 4 (3%) on placebo discontinued treatment prematurely due to adverse events. The OXC-related side effects necessitating drug withdrawal were nausea and vomiting in 5, and rash in 4. (Glauser TA, Nigro M, Sachdeo R et al. Adjunctive therapy with oxcarbazepine in children with partial seizures. <u>Neurology</u> June (2 of 2) 2000;54:2237-2244). (Reprints: Dr Tracy A Glauser, Children's Hospital Medical Center, Department of Neurology, OSB-5, 3333 Burnet Ave, Cincinnati, OH 45229).

COMMENT. Oxcarbazepine is considered effective as an adjunctive antiepileptic therapy in children with inadequately controlled partial seizures.

Oxcarbazepine monotherapy for partial-onset seizures was studied in a multicenter, double-blind trial in outpatients aged 12 years or older with inadequately controlled seizures. (Beydoun A, Sachdeo RC, Rosenfeld WE et al. <u>Neurology</u> June (2 of 2) 2000;54:2245-2251). Patients receiving a higher dosage (2400 mg/day) of OXC were benefited more than those on a lower dose (300 mg/day); 12% seizure-free compared to none, respectively.

SEIZURE DISORDERS

PYRIDOXINE-DEPENDENT EPILEPSY AND PIPECOLIC ACID

Two neonates with pyridoxine-dependent epilepsy and significant elevation of pipecolic acid in plasma and CSF are reported from the University Hospital Vienna, Austria. Diagnosis was based on an immediate control of seizures and clinical response with IV pyridoxine 100 to 300 mg, and continued control of seizures with a maintenance oral dose of 200 mg/day or 10 mg/kg/d. Further increases of CSF pipecolic acid occurred during a 72-hour withdrawal of pyridoxine in 1 patient. Pipecolic acid was continuously elevated in the plasma of the 2 infants with pyridoxine-dependent epilepsy (10 mcmol/L plasma), and was normal in 26 controls with non-pyridoxine-dependent seizures (2 mcmol/L). There was an inverse correlation of pyridoxalphosphate in plasma versus pipecolic acid levels. High pipecolic acid levels are suggested as a diagnostic marker of pyridoxine-dependent epilepsy. (Plecko B, Stockler-Ipsiroglu S, Paschke E et al. Pipecolic acid elevation in plasma and cerebrospinal fluid of two patients with pyridoxine-dependent epilepsy. <u>Ann Neurol</u> July 2000;48:121-125). Wahringergurtel 18-20 A-1090 Vienna, Austria).

COMMENT. Plasma pipecolic acid determination may aid in diagnosis, and a persistent elevation may avoid premature pyridoxine withdrawal in infants with pyridoxine-dependent epilepsy (normal range, 0.7-2.6 mcmol/L). The authors report an additional case of this syndrome in a 7 year-old child.

Pipecolic acid elevation in pyridoxine-dependent epilepsy may be caused by a deficiency of pyridoxal-dependent a-aminoadipic acid transaminase, a step in the degradation of lysine to acetoacetyl-CoA in the brain. Pipecolic acid also accumulates in peroxisomal disorders, such as Zellweger syndrome.

AUTOSOMAL DOMINANT PARTIAL EPILEPSIES

The clinical, electrophysiologic, and genetic characteristics of autosomal dominant partial epilepsy were studied in 71 patients and 33 non-epileptic at-risk family members in 19 European families followed at the Hopital Universitaire de Geneve, Switzerland, and centers in Strasbourg, Paris, Grenoble, Nice, Marseille, Rome, and Pisa. Families were subdivided into those with autosomal dominant nocturnal frontal lobe epilepsy (ADNFLE) (n = 8), familial temporal lobe epilepsy (7), and autosomal dominant partial epilepsy (4).

Familial partial epilepsies show great intrafamilial variability, and up to 30% may be resistant to antiepileptic medication. Some affected family members may have only EEG abnormalities, without clinical seizures, reflecting incomplete penetrance. Genetic studies found no mutation in the a4 and B2 nicotinic acethylcholine receptor subunits, but positive lod scores were obtained in 4 families with markers from the candidate region on chromosome 10q. (Picard F, Baulac S, Kahane P et al. Dominant partial epilepsies. A clinical, electrophysiological and genetic study of 19 European families. <u>Frain</u> June 2000;123:1247-1262). (Respond: Dr Fabienne Picard, EEG, Department of Neurology, Hopital Universitaire de Geneve, 24, rue Michell-du-Crest, 1211 Geneva 14, Switzerland).

COMMENT. Familial partial epilepsies may originate in frontal, temporal, and other variable locations. Clinical and surface EEG findings may provide conflicting localizing evidence, and an overlap of partial epilepsy syndromes within families may occur, with genetic heterogeneity.

Frontal lobe origin of absence seizures is discussed by Pavone A and Niedermeyer E (<u>Clin Electroencephalogr</u> July 2000;31:153-156). The distinction between partial and absence seizures of frontal lobe origin is important from a therapeutic standpoint. Carbamazepine is the agent of choice for partial, and valproate for absence seizures.

HHV-6, INFANTILE SPASMS, AND CEREBELLAR ASTOCYTOMA

A case of human herpesvirus-6 encephalitis, carditis, infantile spasms, and a subsequent cerebellar astrocytoma containing the HHV-6 genome, is reported from the University of Oulu, Finland. A 14-month-old girl presented with fever, hypotonia, and a diffuse urticarial exanthem. After admission, she developed encephalitis and status epilepticus, followed by myocarditis. MRI of the brain showed thin subdural effusions but no tumor. After 11 weeks from onset, convulsions changed to infantile spasms, resistant to vigabatrin and ACTH. A repeat MRI at 11 months after the primary illness showed a cystic astrocytoma located near the vermis. Five months after surgical removal of the tumor, the patient has hypotonia, poor social communication, and daily infantile spasms. HHV-6 DNA was detected by PCR in the tumor tissue. (Rantala H, Mannonen L