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SEIZURE DISORDERS

ACETAZOLAMIDE FOR PARTIAL SEIZURES

Acetazolamide (Diamox) (AZM) was tried as an adjunct to carbamazepine (CBZ) in 48 refractory partial seizure patients, the majority being adults and only 5 under 12 years of age. The seizures were complex partial in 80%, and idiopathic in 67%. A response measured by a 50% reduction in seizure frequency was obtained in 44% of patients, and side effects - lethargy, paresthesias, anorexia - were generally mild or transient. The duration of response ranged from 3 to 30 months and tolerance was not a major problem. Initial effective doses ranged from 3.8 to 16.5 mg/kg/day (mean, 8.2), and the maximum effective dose used was 22 mg/kg/day. The study was retrospective and uncontrolled, but the authors considered their results impressive and recommend AZM in preference to clonazepam as adjunctive therapy for partial seizures. (Oles KS, Penry JK, et al. Use of acetazolamide as an adjunctive to carbamazepine in refractory partial seizures. Epilepsia Jan/Feb 1989;30:74-78).

> COMMENT. Having been an advocate of acetazolamide for the treatment of refractory childhood seizures for several years (Millichap, JG et al. J Pharmacol & Exptl Therap 1955;115:251; Neurology 1956;6:552; Lancet July 18, 1987;2:163), I am happy to see that Dr. Penry and his associates now support its use in adults with partial seizures. AZM had previously been proposed as an alternative agent in the management of petit mal (absence) seizures in children, in menstruation-related seizures, and as an adjunct treatment in other refractory generalized and partial seizures of childhood. Despite the tendency for development of

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tolerance, which is also shared by the benzodiazepine agents, a review of published work in 1967 showed that AZM was equal in efficacy to ethosuximide and had a lower incidence of side effects (Millichap JG, Aymat F. Treatment and prognosis of petit mal epilepsy. Pediatr Clin N Am 1967;14:905). At least as an adjunct therapy, the drug deserves wider recognition and confirmation of efficacy by controlled studies.

SIDE EFFECTS OF ANTICONVULSANT MONOTHERAPY

The severity and nature of side effects and doses and plasma levels of phenobarbital (PB), primidone (PRM), phenytoin (PHT), carbamazepine (CBZ), and valproate (VPA) were examined in 392 pediatric outpatients at the Division of Paediatric Neurology, National Hospital "Marques de Valdecilla", University of Cantabria, Santander, Spain. Side effects occurred in 50%, necessitating changes in medication in 18% and withdrawal of drug in 7%. The incidence of side effects was highest with PHT (71%) and lowest with PRM (29%). Serious side effects requiring drug withdrawal occurred with PHT (10%), VPA (8%), and PRM (8%), and less frequently with PB (4%) and CBZ (3%). The best tolerated drug was CBZ, and the least tolerated was PHT. Behavioral side effects were noted most commonly with PB (60%), neurological abnormalities such as ataxia and nystagmus with PHT (22%), digestive tract disorders with VPA (28%), and gingival hyperplasia and hirsutism with PHT (58%). The side effects that most often necessitated changes in treatment were behavioral disorders, especially excitement and hyperactivity, with PB and PRM, hirsutism and gingival hyperplasia with PHT, restless sleep and vomiting with CBZ, and digestive disorders with VPA. Behavioral disorders produced by PB and PRM disappeared in half of the patients if the dosage of the drug was increased. (Herranz JL et al. Clinical side effects of phenobarbital, primidone, phenytoin, carbamazepine, and valproate during monotherapy in children. Epilepsia Nov/Dec 1988;29:794-804).

COMMENT. A collaborative group for epidemiology of epilepsy reports a 42% incidence of adverse reactions to antiepileptic drugs in 355 patients followed for an average of 11 months in 15 university and hospital centers in Italy (Beghi E et al. Institute for Pharmacological Research "Mario Negri," Milan. Epilepsia Nov/Dec 1988;29:787). Clinical judgment provided the most valid basis for the evaluation of drug toxicity, and "toxic" plasma drug levels were not correlated with adverse reactions. Plasma levels were within normal limits in 78% of cases with and in 81% of cases without adverse drug reactions. Of 31 patients with "abnormal" plasma levels, only 1 had an adverse drug reaction. The authors stress the importance of reporting adverse drug reactions as a means of improving the quality of care for the epileptic in routine clinical practice. Physicians are sometimes reluctant to get involved, fearing legal repercussions or lengthy and tedious questionnaires from drug companies. Perhaps a system permitting anonymity might encourage more active physician participation.