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SEIZURE DISORDERS

VALPROATE AND CARBAMAZEPINE COMPARATIVE TRIAL

The efficacy and side-effects of sodium valproate (VA) and carbamazepine (CBZ) were compared in 260 children (5 to 16 years of age) with primary generalized epilepsy or partial epilepsy followed for three years at 63 outpatient clinics in the UK and Ireland and results were reported from Addenbrooke's Hospital, Cambridge, the Hospital for Sick Children, Great Ormond Street, London, and the Trial Office at Sanofi Winthrop Ltd, Guildford, Surrey, UK. Patients with newly diagnosed epilepsy and at least two seizures in the previous six months were randomized to receive either sodium valproate (200mg twice daily initially, mean maximum 17mg/kg daily) or carbamazepine (5mg/kg initially, mean maximum 10mg/kg daily). Doses were increased until seizures were controlled or toxicity ensued. VA or CBZ was stopped in 12% and 13%, respectively, because of poor seizure control, and in 15% and 12% because of adverse side-effects. Approximately 50% of patients were completely free of seizures for the first 6 months, and 75% had been free for 12 months and 50% for at least two years, by the end of the trial. Primary generalized seizures responded better than partial seizures. VA and CBZ were equally effective; a higher remission rate for VA treated patients was not statistically significant. Most frequent VA side-effects were appetite and weight increase (11%), somnolence (10%), and alopecia (4%). CBZ cf VA caused a higher incidence of somnolence (20% v 10%), diplopia (4% v 0%), ataxia (4% v 0%), and rash (6% v 3%). (Verity CM, Hosking G, Easter DJ. A multicentre comparative trial of sodium valproate and carbamazepine in paediatric epilepsy. Dev Med Child Neurol Feb 1995;37:97-108). (Respond: Dr DJ Easter, Sanofi Winthrop Ltd, One Onslow St, Guildford, Surrey GU1 4YS, UK).

> COMMENT. The incidence and type of side-effects are the main determinants for the choice of anticonvulsant in a particular patient. As with previous reports of comparative trials of phenobarbital, phenytoin, carbamazepine, and sodium valproate in both adults and children, there were no significant differences in efficacy between drugs regardless of seizure type, generalized tonic-clonic or partial.

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However, side-effects with VA and CBZ were significantly different. Weight gain was particularly troublesome with VA, while somnolence, dizziness, and ataxia required modification of dosage of CBZ. Severe rash noted in 10% of patients taking CBZ in previous adult studies necessitated drug withdrawal in only 3% of children in the present report. Carbamazepine-induced skin rash was reported in 10% of 335 children treated at Toyama Medical University, Japan, and additional reports are cited in Progress in Pediatric Neurology II, PNB Publ, 1994, pp107-109.

VIGABATRIN MONOTHERAPY FOR INFANTILE SPASMS

The successful management of 21 children with infantile spasms and hypsarrhythmia using vigabatrin monotherapy is reported from the Alder Hey Children's Hospital, Liverpool, UK. Age at onset of spasms was 3 to 16 months. A symptomatic cause was identified in 17(81%). Spasms were completely controlled in 17(81%) with an initial dose of vigabatrin 25-50 mg/kg/day, increasing to a maximum of 80-120 mg/kg/d in 3-5 days. At a mean 2 year follow-up, 14(67%) remained seizure-free, and vigabatrin was withdrawn in 4 without relapse. Only one patient failed to respond; this child had meningitis at 4 months and spasms were refractory to all AEDs, including ACTH. Transient drowsiness in 2 patients was the only side-effect noted. (Appleton RE. A simple, effective and well-tolerated treatment regime for West syndrome. Dev Med Child Neurol Feb 1995;37:185-187). (Respond: Dr Richard E Appleton, Royal Liverpool Children's NHS Trust, Alder Hey Children's Hospital, Eaton Rd, Liverpool L12 2AP, UK).

COMMENT. Vigabatrin has replaced ACTH and prednisone as the first-line treatment for West syndrome in the Liverpool Children's Hospital. Dr Verity and colleagues in the UK have been very successful in their organization of a multicenter, comparative trial of sodium valproate and carbamazepine. A similar controlled trial of vigabatrin and ACTH based in Liverpool might be necessary to convince other centers to initiate a change in treatment of infantile spasms.

Of interest, only 4 children (10%) were seizure free following vigabatrin monotherapy for intractable epilepsy in a previous report from the Royal Liverpool Children's Hospital. Complex partial seizures responded partially but myoclonic seizures were not benefited.(Gibbs et al. 1992; see Progress in Pediatric Neurology II, 1994, pp 104-5).

An open, add-on trial of vigabatrin in 20 children with Lennox-Gastaut syndrome, reported from Wien, Austria, showed 85% with a 50-100% reduction in seizure frequency, even after valproate dosage was reduced. Dyskinesia in 1 child was the only side-effect. (Feucht M, Brantner-Inthaler S. Epilepsia 1994;35:993). Serious mood disorders, depression and/or aggression, were the main reason for withdrawing vigabatrin in 9 (12%) of 73 adults with refractory epilepsy treated at the Meer & Bosch Epilepsy Centre, Heemstede, The Netherlands. (Aldenkamp AP et al. Epilepsia 1994;35:999). Vigabatrin results in a significant increase in brain GABA concentration by inhibiting GABA transaminase.

THEOPHYLLINE-INDUCED INFANTILE SPASMS

Infantile spasms and hypsarrhythmia developed in a 6-month-old infant with asthma after 3 days treatment with theophylline at the Royal