SEIZURE DISORDERS

VALPROATE AND RISK OF FRACTURE IN RETT SYNDROME

The association between fracture risk and commonly used antiepileptic drugs (AEDs) in 233 cases of Rett syndrome was investigated by researchers at medical centers in Australia. Patients were sourced from the population-based Australian Rett Syndrome Database. After controlling for mobility, epilepsy diagnosis and genotype, use of valproate (n=134, mean age 15.8 years), prescribed alone or with other AEDs, increased the risk of fracture threefold after at least 1 year and after 2 or more years. Lamatrogine (n=100) caused a lesser increase in risk in the first year of use but no increase in subsequent years. Carbamazepine (n=114) slightly decreased the risk of fracture after 2 or more years of use. These effects were present when analyses were repeated using only cases of Rett syndrome with X-linked MECP2 mutations (n=183), with results similar to all cases, including those clinically diagnosed. (Leonard H, Downs J, Jian L et al. Valproate and risk of fracture in Rett syndrome. **Arch Dis Child** June 2010;85:444-448). (Respond: Dr Helen Leonard, Telethon Institute for Child Health Research, University of Western Australia, PO Box 855, West Perth 6872, Western Australia. E-mail: hleonard@ichr.uwa.edu.au).

COMMENT. Rett syndrome is associated with reduced mineral density and a fracture rate, mostly affecting the femur, nearly 4 times that of the general population. Seizures occur in 80% of girls and women with Rett syndrome, and epilepsy increases risk of fracture, especially when treated with valproate for 1 year or longer. Risk is not increased by other AEDs and may be reduced by carbamazepine. Long-term treatment of epilepsy in Rett syndrome patients should favor AEDs other than valproate when possible.

Researchers at Royal Melbourne Hospital and Universities of Melbourne and New South Wales, Australia, have characterized adverse effects of valproate on bone mineralization of various strains of mice identified as either sensitive or resistant. (Senn SM et al. **Epilepsia** June 2010;51:984-993). Bone mineral content was reduced 9.1% and trabecular volumetric density by 10.7% following chronic valproate treatment in mice strains sensitive to AED-induced bone loss. Resistant strains showed no adverse effects of valproate on bone. The strain-specific effects suggest a role of genetic factors in the pathogenesis of AED-induced bone disease.

LONG-TERM FOLLOW-UP OF DRAVET SYNDROME TO ADULTHOOD

Researchers at Department of Child Neurology, Okayama University Hospital, Japan, have followed 31 patients with Dravet syndrome (DS) (14 typical and 17 borderline DS) from childhood to at least 18 years of age. The study began with 37 patients but 6 (16.2%) died in childhood (5–12 years), 3 in status epilepticus. Clinical findings in the 31 typical and borderline cases became largely similar in adolescence and adulthood. Seizures were intractable in childhood, but suppressed in five (16.1%) during