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ANTIPILEPTIC DRUGS

CHILD DEVELOPMENT AFTER FETAL EXPOSURE TO AED

Researchers at the University of Liverpool and the Department of Neurology, Royal Group of Hospitals, Belfast, UK, investigated the early cognitive development of 155 children born to women with epilepsy (WWE) and exposed in utero to the antiepileptic drug, levetiracetam (LEV) or sodium valproate (VPA). For mothers taking LEV throughout pregnancy, the mean dose was 1,700 mg, and for mothers taking VPA, the mean dose was 800 mg. Seizures occurred in 44.1% of WWE during pregnancy. Children recruited prospectively from 2 cohorts were tested using the Griffiths Mental Development Scale (1996) at age <24 months. The overall developmental outcome of children exposed to seizures during pregnancy was not different from those unexposed. Children exposed to LEV (n=95) monotherapy had higher developmental scores when compared to children exposed to VPA (n=60)(p<0.001). On overall development, children exposed to LEV did not differ from control children (n=98)(p=0.62). Only 8% of children exposed to LEV had below average developmental quotients (DQ<84) compared to 40% of children exposed to VPA. LEV exposure was associated with higher scores for overall DQ (p<0.001), when compared with VPA exposure. After controlling for confounding factors (eg seizures, maternal IQ, maternal and child age), children exposed to LEV in utero are not at increased risk of delayed early cognitive development under the age of 24 months. (Shallcross R, Bromley RL, Irwin B, et al. Child development following in utero exposure. Levetiracetam vs sodium valproate. *Neurology* Jan 25, 2011;76:383-389).(Response and reprints: Prof Gus Baker, Department of Neurological Sciences, Clinical Science Centre for Research, Lower Lane, Liverpool, L9 7LJ UK. E-mail: g.baker@liv.ac.uk).

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COMMENT. Cognitive development of children exposed in utero to LEV is not delayed under age 24 months. Testing of cognitive outcome in school-age children is indicated to exclude longer-term effects of in utero exposure to partial LEV. Childhood exposure (ages 4-16 years) to LEV as adjunctive therapy for partial seizures in 46 patients vs 27 taking placebo found no significant differences in neurocognitive effects. LEV was effective and well tolerated. (Levisohn PM, Mintz M, Hunter SJ et al. LEV Study Group. **Epilepsia** 2009;50(11):2377-2389). LEV is indicated as adjunctive therapy for partial seizures (Browne TR, Holmes GL, 2004) and is also effective in children with generalized seizures (Lee YJ et al. **Pediatr Neurol** 2010;42(2):86-92). Drowsiness, dizziness, behavioral problems, and irritability are reported side effects, but they rarely require drug withdrawal.

Efficacy and tolerability of levetiracetam in children with epilepsy. (Li J, Xiao N, Chen S. **Brain Dev** Feb 2011;33:154-151). In a prospective trial of levetiracetam in 120 children (mean age 4.5 +/- 3.9 years) with partial (44%) and generalized (29%) seizures, 65% were seizure free, and 83% had a seizure reduction of >50%. Patients with infantile spasms (n=15) had complete seizure control in 40%. Average duration of follow-up was 10.3 +/- 3.5 months. Side effects included somnolence, nervousness, and dysphoria in 47%, and 4% discontinued treatment because of side effects. One-year retention rate of levetiracetam was 73%, similar to that in a previous large study cohort (Despondt C et al. *J Neurol Neurosurg Psychiatry* 2006;77:10-13).

VERBAL VS NON-VERBAL COGNITIVE OUTCOMES AT 3 YEARS AFTER FETAL AED EXPOSURE

Verbal and non-verbal cognitive abilities were assessed at 3 years of age in 216 children exposed in utero to commonly used antiepileptic drugs. The investigation was an ongoing prospective multicenter study in the USA and UK, involving pregnant females with epilepsy on monotherapy with carbamazepine, lamotrigine, phenytoin or valproate, from 1999 to 2004. Tests included Differential Ability Scales, Preschool Language Scale, Peabody Picture Vocabulary Test and Developmental Test of Visual-Motor Integration. Verbal scores were lower than non-verbal in children exposed to each drug. They were higher if mother received preconceptional folate. Valproate was associated with poorer cognitive outcomes, both verbal and non-verbal, and the negative effect was dose related. Carbamazepine had a negative, dose related effect on verbal performance. Effects of lamotrigine and phenytoin on cognitive performance were not dose related. Fetal AED exposure may alter language development and normal cerebral lateralization. Preconceptional folate may improve cognitive outcomes. (Meador KJ, Baker GA, Browning N, et al. Foetal antiepileptic drug exposure and verbal versus non-verbal abilities at three years of age. **Brain** Feb 2011;134:396-404). (Respond: Kimford J Meador MD, Department of Neurology, Emory University, 101 Woodruff Circle, Suite 6000, Atlanta, GA 30322. E-mail: kimford.meador@emory.edu).

COMMENT. This study provides further evidence of the adverse cognitive outcome in young children exposed to some common AEDs in utero, and the negative dose related effects on both verbal and non-verbal performance associated with fetal