GABA enhancing antiepileptic drug safer for human developing vs. mature retina

Purpose: Infantile spasms (IS) is an age-specific epilepsy. The GABA enhancing drug vigabatrin (VGB) is used commonly for treatment. 30-40% adults incur vigabatrin attributed visual toxicity expressed as concentric visual field constriction. The surrogate marker for vigabatrin attributed toxicity in infants is reduction of cone ERG 30Hz flicker amplitude. Our purpose was to determine, in human infants, if age of onset of vigabatrin treatment contributes to the incidence of retinal toxicity and if there are visual correlates to toxicity. Methods: Prospective, longitudinal study including 130 patients with infantile spasms treated with VGB (age drug started 1-15 months of age). Sequential ERGs (ISCEV standards) were recorded at 3 or 6 month intervals. Contrast sensitivity and grating acuity were assessed with sweep visual evoked potentials. All data were age-corrected. Results: Sustained reduction of 30 Hz flicker was evident in approximately 1/3 of this cohort. The highest prevalence of ERG dysfunction was in those treated after 6 vs. less than 6 months of age. At baseline (before drug treatment) contrast sensitivity was reduced. Reduced grating acuity was associated with presence of retinal toxicity. Discussion: IS may be associated with less GABA in the CNS during early development. The lowered GABA levels might be associated with less lateral inhibition and reduced contrast sensitivity. Early treatment with VGB increases GABA in the brain and retina possibly compensating for early GABA deficiency. Later treatment may be associated with increased levels of retinal GABA which might be a contributing factor to VGB attributed toxicity. Retinal toxicity is identified by reduced cone system defect. Reduced grating acuity associated with retinal toxicity may be attributed to cone dysfunction during the first year of life when rapid retinal and acuity development occurs.

Carol Westall
The Hospital for Sick Children