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INFANTILE-ONSET SEIZURES

SEIZURE OUTCOME IN INFANTILE SPASMS

Researchers at Great Ormond Street Hospital, London, and Lingfield Centre for Epilepsy, Surrey, UK, studied retrospectively the seizure outcome of 75 children treated over an 8-year period for infantile spasms (IS) with prednisolone or vigabatrin. Prior to the UK Infantile Spasms Study (UKISS) (Lux et al, 2004) vigabatrin was the treatment of choice at this institution; after the study, steroids were preferred. Of 75 children treated, 24 (32%) had cryptogenic and 51 (68%) had symptomatic spasms. Mean age at onset of IS was 6 months. Response to therapy was defined as complete absence of spasms for at least 2 weeks. EEG was not used to categorize response.

IS response rate was 61.1% with steroid therapy and 42.5% with vigabatrin. Response was faster with steroids than vigabatrin, but relapse rates were similar for both. Response to first-line therapy is the main predictor of long-term seizure outcome. Of 51 requiring a second line therapy, 31 received steroids (29 a combination of vigabatrin and steroids) with a response rate of 51.6% (48.2% in the combined group). Of 11 patients receiving vigabatrin as second line therapy, 45.4% responded. Combination therapy was no more effective than vigabatrin alone ($p>0.05$). Cryptogenic seizures responded significantly better to steroids (100% response rate) and had a better neurodevelopmental outcome ($p=0.01$), whereas the symptomatic group responded to vigabatrin (48.7%) or steroids (22.2%) only partially ($p>0.05$). Time to treatment (< or > 28 days of onset) did not influence seizure or developmental outcome. At 12 months follow-up, 78% children with spasms had seizures of other types. (Mohamed BP, Scott RC, Desai N, Gutta P, Patil S. Seizure outcome in infantile spasms – a retrospective study. **Epilepsia** April 2011;52(4):746-752). (Respond: Dr Patil, Dept of Neurosciences, Great Ormond Street Hospital for Children, London WC1N 3JH. E-mail: spatil74@rediffmail.com).

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COMMENT. Since the first report of the effectiveness of ACTH by Sorel et al in 1958, the optimal treatment for infantile spasms is still unclear. ACTH is generally considered superior, and the use of prednisolone in the above study may account for some differences in response. Also, lack of EEG monitoring may have altered the observed response rates. For example, in contrast to the present report, previous studies have shown that the earlier the treatment, younger the patient, and higher the developmental quotient, the better the seizure and EEG outcome. (Millichap, Bickford. **JAMA** 1962;182:523-527; Koo et al. **Neurology** 1993;43:2322-2327).

In agreement with previous studies, the Great Ormond Street Hospital experience shows that cryptogenic in contrast to symptomatic spasms have 100% response to treatment and a good neurodevelopmental outcome. The authors conclude that steroids are the initial treatment of choice for infantile spasms, except for patients with tuberous sclerosis who respond to vigabatrin. That spasms are controlled faster with steroids than vigabatrin is a potential advantage, if the length of exposure to seizures and EEG hypsarrhythmia predicts cognitive outcome. Relapse rates with steroids or vigabatrin are similar. Combination, vigabatrin and steroid, a potential second-line therapy is not more effective than steroid or vigabatrin alone, but a larger controlled study may be indicated.

Add-on ketogenic diet. Short-term use (8 months) of the ketogenic diet 3:1 ratio as add-on treatment was successful in control of infantile spasms and hypsarrhythmia in 14 of 16 patients, without the growth disturbance that occurs with the traditional long-term (2 years) ketogenic diet. (Kang H-C, et al. **Epilepsia** 2011;52(4):781-787).

BRAIN ALKALOSIS AND BIRTH ASPHYXIA SEIZURES

Researchers at University of Helsinki, Finland, studied the causal mechanisms of seizures associated with birth asphyxia using 6 day-old rat pups exposed for 1 hour to hypercapnia (20% CO2 in inhaled gas), hypoxia (9% O2), or both (asphyxic conditions). Normocapnia was restored gradually using CO2 levels of 10% and 5%. Loss of righting reflex was used to indicate the severest expression of neonatal seizure and to quantify the seizure burden during 2-hour observation following asphyxia. Intracranial EEG was also utilized. The effect of postexposure changes in brain pH on seizure burden was assessed after restoration of normoxia and normocapnia. Hypercapnia or hypoxia alone had little effect on seizure burden, but rapid recovery from asphyxia was followed by a large seizure burden that paralleled a rise in brain pH, but no change in brain oxygenation. The seizure burden and alkaline shift in brain pH were strongly suppressed by a graded restoration of normocapnia after asphyxia. Preapplication of N-methyl-isobutyl-amiloride, an inhibitor of Na+/H+ exchanger, blocked seizures completely. Brain alkalosis after recovery from birth asphyxia has a key role in the triggering of seizures. The rapid restoration of normocapnia in the immediate postasphyxia period should be avoided and a graded restoration of brain pH implemented. (Helmy MM, Tolner EA, Vanhatalo S, Voipio J, Kaila K. Brain alkalosis causes birth asphyxia seizures, suggesting therapeutic strategy. **Ann Neurol** April 2011;69:493-500). (Respond: Dr Kaila, Dept Biosciences, PO Box 65, 00014 University of Helsinki, Helsinki, Finland. E-mail: kai.kaila@helsinki.fi).