

Faulkner S, Fleiss B, et al. Melatonin augments hypothermic neuroprotection in a perinatal asphyxia model. **Brain** 2013 Jan;136(Pt 1):90-105). (Response: Dr Nicola J Robertson. E-mail: n.robertson@ucl.ac.uk).

COMMENT. Melatonin (N-acetyl-5-methoxytryptamine), a naturally occurring hormone secreted by the pineal gland, when administered alone has neuroprotective actions against H-I brain injury in animal models. The present study demonstrates that melatonin augments the neuroprotective effect of hypothermia.

Potential synergistic neuroprotective therapies with hypothermia include inhaled xenon, N-acetylcysteine, erythropoietin, anticonvulsants and cannabinoids, in addition to melatonin. (Cilio MR, Ferriero DM. **Semin Fetal Neonatal Med** 2010 Oct;15(5):293-8) (Kelen D, Robertson NJ. **Early Hum Dev** 2010 Jun;86(6):369-77).

SEIZURE DISORDERS

PROGNOSTIC FACTORS FOR REFRACTORY STATUS EPILEPTICUS

Researchers at the Mayo Clinic, Rochester, MN studied the outcome and identified prognostic factors for refractory status epilepticus (RSE) in 54 adult patients, median age 52 years [range 18-93]. RSE was defined as generalized convulsive or nonconvulsive status epilepticus that continued despite initial first and second-line therapies. Patients younger than 18 years, anoxic/myoclonic, psychogenic, simple partial, and absence SE were excluded. Of 63 consecutive episodes of RSE, anesthetic agents were used in 55 (87.3%). Duration of drug-induced coma was a mean of 11 days (SD 17.9 days). Cardiac arrhythmias occurred in 21 of 60 episodes (35%) and required intervention in 14 of 21 cases (66.67%). In hospital mortality was 31.75%, in 20 of 63 episodes. Functional outcome at discharge was poor in 48 (76.19%) episodes. Hospital length of stay was a mean of 27.7 days (SD 37.3 days). Poor functional outcome was associated with drug-induced coma (p=0.03), cardiac arrhythmias requiring intervention (p=0.01), and pneumonia (p=0.01). Prolonged mechanical ventilation was associated with mortality (p=0.04). Good functional recovery (p=0.01) followed seizure control without suppression-burst or isoelectric EEG. Functional outcome was not related to age, history of epilepsy, previous SE, type of SE, and anesthetic drug used. (Hocker SF, Britton JW, Mandrekar JN, Wijdicks EFM, Rabinstein AA. Predictors of outcome in refractory status epilepticus. **JAMA Neurol** 2013 Jan 1;70(1):72-7). (Response: Sara E Hocker MD, Department of Neurology, Mayo Clinic, 200 First St SW, Rochester, MN 55905. E-mail: Hocker.sara@mayo.edu).

COMMENT. In adults with refractory status epilepticus, risk factors for a poor prognosis include the severity of the SE, the need for drug-induced coma, cardiopulmonary complications requiring prolonged mechanical ventilation, and pneumonia. Aggressive EEG suppression does not improve outcome of RSE. Three-quarters of adult RSE patients have a poor outcome.

A review of studies of status epilepticus published from 1990-2009 shows that children have a better prognosis than adults, and age and depth of coma are the strongest

predictors of outcome of SE. (Neligan A, Shorvon SD. Prognostic factors, morbidity and mortality in tonic-clonic status epilepticus: a review. **Epilepsy Res** 2011 Jan;93(1):1-10). In otherwise normal children with focal epilepsy, SE has no significant effect on long-term intellectual and seizure outcome. (Camfield P, Camfield C. **Pediatrics** 2012 Sep;130(3):e501-6).

CLINICAL, BIOCHEMICAL, AND MOLECULAR STUDIES AND TREATMENT OF PYRIDOXINE-DEPENDENT EPILEPSY

Researchers at Autonomous University of Madrid, and other centers in Spain studied the clinical, biochemical, and genetic spectrum of pyridoxine-dependent epilepsy (PDE) in 12 patients with the clinically proven diagnosis. Onset of seizures varied from neonatal to first months of life. Seizures were focal or multifocal, clonic or myoclonic, and generalized tonic; 50% had status epilepticus. Seizures were controlled transiently with conventional AEDs for 15 or more days in 8 of 12 patients, leading to a delay in diagnosis. The effective dose of pyridoxine to suppress seizures ranged from 10 to 30 mg/kg/day. Neurologic symptoms in addition to seizures included hypotonia, irritability, and psychomotor retardation. EEG abnormalities were variable and included focal or multifocal discharges, burst-suppression pattern, and generalized slowing. A normal EEG in one patient does not rule out the diagnosis. All EEGs became normal after pyridoxine therapy. MRI abnormalities, mainly posterior fossa, included mega cisterna magna, Dandy Walker syndrome, ventriculomegaly, and corpus callosum dysgenesis. Six patients followed for more than 5 years show cognitive dysfunction and borderline or mildly retarded IQs. Delay in treatment and dysgenesis of the corpus callosum are risk factors for neurodevelopmental delay. Treatment with pyridoxine does not normalize the IQ. Urine levels of α -aminoadipic semialdehyde (α -AASA) and plasma/CSF levels of pipercolic acid (PA) are diagnostic biomarkers. Genetic analysis of these Spanish patients showed 12 mutations, 7 novel, and different from other populations. (Perez B, Gutierrez-Solana LG, Verdu A, et al. Clinical, Biochemical, and molecular studies in pyridoxine-dependent epilepsy: Antisense therapy as possible new therapeutic option. **Epilepsia** 2013 Feb;54(2):239-48). (Response: Dr Belen Perez. E-mail: bperez@cbm.uam.es).

COMMENT. PDE should be considered in any infant with intractable seizures, including patients with MRI abnormalities such as corpus callosum dysgenesis or Dandy Walker syndrome. The long-term outcome of PDE was poor in a Dutch PDE cohort of 14 patients. (Bok LA, Halbertsma FJ, Houterman S, et al. **Dev Med Child Neurol** 2012 Sep;54(9):849-54). EEG background and epileptiform activity were not correlated with outcome. Delayed initiation of pyridoxine and the association of corpus callosum abnormalities were significantly associated with unfavorable neurodevelopmental outcome, findings similar to the Spanish experience.

PDE WITH MOLYBDENUM COFACTOR DEFICIENCY

PDE with molybdenum cofactor deficiency is reported in 2 siblings. Molecular investigations revealed a homozygous mutation in the MOCS2 gene. Pyridoxine supplementation is recommended in patients diagnosed with molybdenum cofactor or