SEIZURE DISORDERS

PROPHYLACTIC PHENOBARBITAL AFTER RESOLUTION OF NEONATAL SEIZURES

The degree of practice variation in continuance of phenobarbital treatment despite resolution of neonatal seizures was evaluated by national survey conducted at the University of Rochester Medical Center, New York. Surveys mailed to 609 randomly selected child neurologists and 579 neonatologists were completed by 20.7% and 23.1%, respectively. Practices varied widely, with little difference in response frequencies between child neurologists and neonatologists. For child neurologists, prophylactic phenobarbital was always used in 5%, sometimes used in 72%, rarely in 19%, and never in 3%. Responses of neonatologists were similar. Duration of treatment was <1 month in 8%, 1-3 months in 45%, 3-6 months in 37%, none longer than 6 months. Drug levels were monitored routinely by 34%, and only when indicated by 57%. Physicians were more likely to respond yes to continuation of treatment for a given scenario than would be predicted by their overall responses to questions. Since the survey of practices 15 years ago, physicians are reporting less frequent and shorter phenobarbital treatment after resolution of neonatal seizures. (Guillet R, Kwon JM. Prophylactic phenobarbital administration after resolution of neonatal seizures: survey of current practice. **Pediatrics** Oct 2008;122:731-735). (Respond: Ronnie Guillet MD, PhD. E-mail: Ronnie_guillet@urmc.rochester.edu).

COMMENT. The relatively low response to this survey and surveys in general is explained by the length and complexity of questions, and the increasing number of similar requests. Possible late cognitive effects of long-term phenobarbital in the infant are one reason to limit duration of prophylactic treatment. A randomized trial is needed to determine benefits and adverse effects of continued therapy after discharge from the NICU.

PREVENTION OF STATUS EPILEPTICUS IN DRAVET SYNDROME: NATIONWIDE SURVEY IN JAPAN

Child neurologists and epileptologists at various university centers in Japan were surveyed by questionnaire to identify the most effective strategies for management of and prophylaxis against status epilepticus (SE) in children with severe myoclonic epilepsy in infancy (SMEI; Dravet syndrome), especially when associated with fever. Data from 109 patients were analyzed (51 males, 58 females; mean age 10.7 years +/- 6.53; range 1-37 years). Ten had no SE and were excluded. Anticonvulsants with excellent efficacy against SE occurrence were potassium bromide (41.7%), zonisamide (13.5%), clobazam (10%), valproate (8%), phenobarbital (6.7%), and phenytoin (2.6%). Clonazepam and carbamazepine were ineffective. Diazepam suppository was most frequently used against SE triggered by fever, but was effective in only 2.4% cases. Intravenous medications most effective in terminating ongoing SE were barbiturates (75-100%), midazolam (68.8%), diazepam (54.3%), lidocaine (21.4%), and phenytoin (15.4%). (Tanabe T, Awaya Y, Matsuishi T, et al. Management of and prophylaxis against status epilepticus in children with severe myoclonic epilepsy in infancy (SMEI; Dravet syndrome) – A nationwide

questionnaire survey in Japan. **Brain Dev** Nov 2008;30:629-635). (Respond: T Tanabe. E-mail: tanabemapa@pop01.odn.ne.jp).

COMMENT. The use of bromides for treatment of SMEI and their significantly higher efficacy than that of valproic acid and zonisamide are interesting and surprising observations. Bromides were first introduced for the treatment of epilepsy in 1853 (Locock C. **Lancet** May 23, 1857;527). After phenobarbital became available in 1912 and phenytoin in 1937, the use of bromides was largely discontinued. The administration of bromides is not as simple as that of newer anticonvulsant drugs. Its effectiveness depends on a lowered intake of sodium chloride in the diet. The onset of action is delayed for 2 to 3 weeks, and high blood levels are maintained for 1 to 2 weeks after bromides are discontinued. Unlike other anticonvulsants, an abrupt withdrawal of bromides is unlikely to precipitate status epilepticus.

Bromides are usually administered in liquid or tablet forms of sodium bromide or as triple bromide elixir, containing 400 mg each of sodium, potassium and ammonium bromide per 5ml. (Livingston S et al. **Amer J Dis Child** 1953;86:717-720)(Goodman LS, Gilman A. **The Pharmacological Basis of Therapeutics.** New York. Macmillan, 1955;156-163). Suggested starting and maintenance doses of bromides are as follows: For children under 3 years old, 160 mg 2x daily (maximum 320 mg 3x daily); 3 to 6 years old, 320 mg 2x daily (maximum 640 mg 3x daily). (Livingston S. **Comprehensive Management of Epilepsy in Infancy, Childhood and Adolescence.** Springfield, IL. Charles C Thomas, 1972;198, 268-274). A satisfactory blood level of bromides is generally 20 to 25 mEq/L (160 to 200 mg%). Drowsiness and cutaneous reactions are the most troublesome side effects. Administration of extra sodium chloride and fluids usually alleviates drowsiness. Acneiform rashes are a frequent occurrence in adolescents and adults, but are uncommon in infants and young children. Granulomatous lesions (bromoderma) will occur occasionally, taking months to disappear after bromide withdrawal.

Epileptic syndromes with high rates of status epilepticus, in addition to SMEI, include Panayiotopoulos syndrome and symptomatic occipital lobe epilepsy secondary to neonatal hypoglycemia (Okanishi T et al. **Brain Dev** Nov 2008;30:624-628).

RISK OF EPILEPSY IN OFFSPRING EXPOSED TO PREECLAMPSIA OR ECLAMPSIA

Researchers at the University of Aarhus, Denmark, and at centers in China and US, conducted a population-based study of singletons born in Denmark (1978-2004) with information on preeclampsia and epilepsy obtained from the Danish National Hospital Register. They identified 2.9% of children exposed to preeclampsia, and 0.04% to eclampsia during prenatal life. The incidence of epilepsy at 27-year follow-up was increased following exposure to either preeclampsia or eclampsia in children born after 37 weeks of gestation. Children born preterm showed no association between preeclampsia and epilepsy. In contrast, the incidence rate ratios were 1.29 for children born at term and 5.03 for children born postterm. (Wu CS, Sun Y, Vestergaard M, et al. Preeclampsia and risk for epilepsy in offspring. **Pediatrics** Nov 2008;122:1072-1078). (Respond: Chun Sen Wu MD, E-mail: cw@soci.au.dk).