

NEONATAL INTRACTABLE SEIZURES AND VALPROIC ACID THERAPY

Seizures resistant to phenobarbital were controlled in four of six neonates by valproic acid (VPA) monotherapy and in one with polytherapy at the Moses H Cone Memorial Hospital, Greensboro, NC. The pharmacokinetics of VPA showed a prolonged half-life in neonates in contrast to the short half-life in older children and adults. A loading dose of 20 mg/kg followed by a maintenance dose of 10 mg/kg every 12 hrs was recommended until VPA clearance and serum levels are determined.

VPA-induced hyperammonemia in all six patients was reason to discontinue VPA in three. One patient with meningitis whose seizures were unresponsive to VPA died shortly after the drug was discontinued; a serum ammonia elevation to 900 umol/l after 5 days of treatment returned to normal with 24-48 hrs after discontinuing the drug. (Gal P, Weaver R et al. Valproic acid efficacy, toxicity, and pharmacokinetics in neonates with intractable seizures. Neurology March 1988;38:467-71).

COMMENT. VPA toxicity, particularly hepatotoxicity, in infants and young children may be reduced in frequency by elimination of concurrent anticonvulsants, but serum ammonia must be closely monitored even with monotherapy. Cerebral edema, increased intracranial pressure, cytotoxic changes in the brain and coma are reported with hyperammonemia exceeding 500 umol/l in neonates, and intellectual retardation and brain damage are correlated with duration of hyperammonemia and coma (Msall M et al. N Engl J Med 1984;310:1500). Animal experiments show that VPA-induced hyperammonemia is caused primarily by impairment of hepatic intramitochondrial citrullinogenesis, and the renal contribution to systemic hyperammonemia is small (Marini AM et al. Neurology March 1988;38:365).

Brown JK, at the Royal Hospital for Sick Children, Edinburgh, writing on valproate toxicity in Developmental Medicine and Child Neurology (Feb 1988;30:121), cautions that any congenital inborn error of metabolism that affects mitochondrial function or any acquired mitochondriopathy might be expected to increase the risk of serious valproate toxicity in the neonate, and VPA is not generally recommended in the newborn period. He stresses the need for detailed investigation of cases of hepatopathy, including a full screen of mitochondrial enzyme function, as well as histology for possibly Reye-type changes, before accepting a diagnosis of VPA-induced hepatotoxicity.

SEIZURES FOLLOWING DTP IMMUNIZATION

The incidence of seizures following the administration of DTP vaccine at the Group Health Cooperative of Puget Sound, Seattle, has been estimated by epidemiologists at the Harvard School of Public Health, Boston, and by the Boston Collaborative Drug Surveillance Program, Waltham, Mass. For a population of children born in GHC hospitals, 1972-83, records of hospitalizations for neurologic disease and prescriptions of common anticonvulsant drugs were reviewed to establish the probable nature of the illness, the date of its onset, and the temporal relation to DTP.

Children omitted from the study for various reasons were as follows: 1) those not hospitalized nor treated with drug therapy (e.g., uncomplicated first febrile seizures and children with infantile spasms who received only ACTH and steroids as outpatients); 2) those with seizures and a history of possible predisposition due to trauma, asphyxia, malformation, metabolic defect, premature birth, CNS infection and sepsis; 3) those without a clear date of onset for the seizures or neurologic illness; 4) 8 cases of seizures

beginning before immunization in the first 30 days of life; 5) 8 cases with a history of first seizures recorded at a subsequent visit; and 6) 2 cases of infantile spasms and 5 acute encephalopathies with onset recorded 30 days or more after DTP immunization.

Of 231 post-immunization first seizures selected for study without other predisposing cause in children 30 days of age or older, 55 had afebrile seizures, and 176 had febrile seizures. The incidence of recorded febrile seizures in the immediate post-immunization period was 3.7 times that in the period 30 days or more after immunization. One child suffered a prolonged status epilepticus on the evening of her third DTP shot, and neurologic sequelae included focal epilepsy at 6-yr follow-up. Six cases of first seizures occurred within 30 days of immunization, and the expected incidence without immunization in this time interval was calculated at 5.07. The authors conclude that serious neurologic sequelae of DTP immunization are extremely infrequent in otherwise healthy children. (Walker AM et al. Neurologic events following diphtheria-tetanus-pertussis immunization. Pediatrics March 1988;81:345-9).

COMMENT. The omission of several groups of children from this retrospective epidemiological study detracts from the significance of the conclusions and estimates of incidence of DTP-related febrile and non-febrile seizures. The role of DTP as a precipitating cause in children with a predisposition to seizures and as a possible cause of infantile spasms is neglected. It is unfortunate that the study did not address the known risks of DTP in children with prior neurologic disease or predisposition to seizures including positive family history (see Ped Neur Briefs Nov 1987;1:40).

INFANTILE SPASMS

Four infants with partial seizures evolving to infantile spasms were investigated using simultaneous EEG-video-telemetry recording in the Dept of Pediatrics, Nagoya University, Nagoya, and Division of Pediatric Neurology, Central Hospital, Aichi Prefectural Colony, Kasugai, Japan. Partial seizures were characterized by cessation of activity, staring, flushing, automatisms, increased tone and laughter. (Yamamoto N, Watanabe K et al. Partial seizures evolving to infantile spasms. Epilepsia Jan/Feb 1988;29:34-40).

COMMENT. A cry or scream is the most common ictal element in infantile spasms, and laughter and a frightened or confused expression, manifestations of partial seizures, are frequently described (Jeavons PM, Bower BD. Clinics in Developmental Medicine No 15, 1964, London, Spastics Society and Heinemann). The above report appears to be the first in which infantile spasms were preceded by partial seizures confirmed by EEG-VT. However, one of the above authors, in a previous study of the evolution of EEG abnormalities accompanying infantile spasms, reported hypsarrhythmia preceded by focal sharp wave patterns, compatible with partial seizures (Watanabe K et al. Dev Med Child Neurol 1973;15:584).

REFLEX EPILEPSY

HOT WATER EPILEPSY (HWE)

Seizures precipitated by very hot water-head baths (40-50° C), a regional religious custom, or showers were seen in 279 patients between 1980-83 in Bangalore, Southern India, and are reported from the Depts of Neurology and