
SEIZURE DISORDERS

PHENYTOIN FOR POST-TRAUMATIC SEIZURES

A randomized, double-blind study of phenytoin was conducted in 404 patients with serious head trauma at the Departments of Neurological Surgery, Rehabilitation Medicine and Medicine, University of Washington, Seattle. An intravenous loading dose of phenytoin was given within 24 hours of injury to 208 patients and 196 received placebo for a one year period in a double-blind fashion. Serum levels were maintained in the high therapeutic range (3-6 mmol/l). Statistical analyses were performed according to the intention to treat and based on efficacy. Between the initial drug loading dose and day seven, 3.6% of patients assigned to phenytoin had seizures compared to 14% of patients assigned to placebo (P<0.001). From day eight to the end of year one and the end of year two of the study, there was no significant difference between the seizure incidence in the phenytoin and placebo groups, approximately 1 in 5 having a recurrence. The relapse was not explained by low phenytoin levels. (Temkin NR et al. A randomized, double-blind study of phenytoin for the prevention of post-traumatic seizures. N Engl J Med August 23, 1990; 323:497-502).

COMMENT. The authors concluded that phenytoin exerts a beneficial effect by reducing posttraumatic seizures only during the first week after severe head injury. Dr. Allen Hauser, in an editorial comment, states that early administration of loading doses of IV phenytoin to patients with severe head injury may be warranted to prevent early seizures and their complications, but prolonged therapy after stabilization does not seem justified. Other anticonvulsants such as phenobarbital and benzodiazepines should be considered as alternatives, and treatment with antioxidants which reduce edema and prevent neuronal damage caused by iron salts deposited at the time of injury may be of benefit.

FETAL ANTICONVULSANT SYNDROME WITH NECEREBELLAR HYPOPLASIA

An infant with dysmorphic features and hypoplasia of the cerebral hemispheres and cerebellum is reported from the John Radcliffe Hospital, Oxford, England as an extreme example of anticonvulsant teratogenicity. The mother was epileptic and she had taken phenytoin and sodium valproate throughout pregnancy. The infant was cyanosed and hypotonic at birth with Apgar scores of 4 at one minute and 6 at five minutes. She had abnormalities of the toes, fingers, nails, elbows, hips, ears, and an antimongoloid slant to the eyes with hypertelorism. Intractable seizures began ten minutes after delivery and she died at 66 hours of age. Postmortem neuropathological examination showed a thickened skull, reduced size of the pons and neocerebellum and

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COMMENT. The authors felt that this clinical picture may represent the most severe end of the spectrum of fetal abnormalities attributable to phenytoin and/or sodium valproate. The anticonvulsant drug dosages taken by the mother were phenytoin 175 mg and sodium valproate 1 gram daily but the serum levels were not reported.

ACIH IN INFANTILE SPASMS

The relationship between dose of ACTH and the initial effect and long-term prognosis was investigated in 41 children with infantile spasms at the Department of Pediatrics, Kyoto University, Kyoto, Japan. ACTH therapy began at 2-13 months of age (mean: 11.8 months) and the average treatment lag was 4.5 months. All patients were treated with Vitamin B6, valproate, and other anticonvulsants without benefit before ACTH therapy was begun. All patients had hypsarrhythmia on the EEG. The cause was acquired in 30 patients, unknown in 8 and associated with developmental delay, and idiopathic in 3 patients whose development was normal. The doses in 16 patients was 0.5 mg (20 IU) for those older than one year of age and 0.25 mg (10 IU) for those less than one year; daily injections were given for two weeks, every other day for two weeks, and twice weekly for a total of 30 injections. One-half of these doses were used in 14 patients and doses were calculated on the basis of body weight (0.01-0.015 mg) (0.4-0.6 IU)/kg in 11 patients. More than 0.015 mg (0.6 IU)/kg/day of ACTH was needed for a good initial response of seizures and EEG abnormalities. Doses lower than 0.015 mg/kg/day provided less seizure control at the end of treatment and less EEG improvement. ACTH in a dose of 1.6-2.4 IU/kg/day and a total dose of 44-60 IU/kg resulted in better mental development than smaller doses, but side effects increased with larger daily doses or larger total doses. Seizures were controlled in 71-89% with doses above 0.6 IU/kg/day. ACTH-induced cerebral atrophy increased with the total dose of ACTH but was not seen when daily doses were 2.4 IU/kg/day or less and total dose was 60 IU/kg. (Ito M et al. ACTH therapy in infantile spasms: Relationship between dose of ACTH and initial effect or long-term prognosis. Pediatr Neurol July/Aug 1990; 6:240-244).

COMMENT. The authors recommend that ACTH doses based on body weight or body surface area should be used in future studies to compare the results obtained at different institutions. The doses used in this study from Japan were relatively small and ranged from 7.3-47.6 IU/m²/day whereas those recommended in some recent publications have been much higher and usually 150 U/m²/day. Snead OC (Pediatr Neurol May/June 1990; 6:147) advocated 150 U/m²/day for one week, 75 U/m²/day in the second week, and 75 U/m² on alternate days for the third week. Bobele GB, Bodensteiner JB from the University of Oklahoma and Morgantown,