ANTIEPILEPTIC DRUGS

PHENYTOIN AND FOLIC ACID

The pharmacokinetics of phenytoin (PHT) before and after administration of 1 and 5 mg of folic acid is reported from the Colleges of Pharmacy and Medicine, University of Iowa, Iowa City and University of Health Sciences/The Chicago Medical School, Chicago, IL. The measured total serum PHT concentration was always greater than the calculated concentration and the days to the steady state concentration were always longer than the number calculated before folic acid was given. All subjects showed decreased serum folic acid following PHT. Since folate is assumed to be a co-factor in PHT metabolism, these results were expected because depletion of the vitamin would result in reduced metabolism of PHT and higher total serum PHT and longer time to reach steady state. When folic acid was added the same results were obtained. The depletion of folic acid had to be corrected first before its role as a co-factor in PHT metabolism could be used. (Berg MJ et al. Phenytoin pharmacokinetics: before and after folic acid administration. Epilepsia July/Aug 1992; 33:712-20.) (Reprints: Dr. M.J. Berg, College of Pharmacy, University of Iowa, Iowa City, IA 52242.)

COMMENT. The authors suggest that folic acid should be prescribed when phenytoin therapy is initiated.

CARBAMAZEPINE ACUTE TOXICITY

The clinical toxic effects and serum concentrations after ingestion of carbamazepine are reported in 82 pediatric patients from the Intensive Care Unit, Royal Children's Hospital, Melbourne, Australia. Two died, 1 of cardiac failure and 1 of aspiration pneumonitis with septicemia. In 10 patients in deep coma with a Glasgow Coma Scale (GCS) of 3-4, the mean serum level was 213 *u*mol/L. The serum carbamazepine level was related to the depth of coma, convulsions, hypotension caused by myocardial failure and conduction defects, and to the requirement for mechanical ventilation. In 27 patients with moderate coma (GCS 5-8) the mean serum level of carbamazepine was 112 *u*mol/L; convulsions occurred in 2 patients in this group. In 45 patients with mildly depressed consciousness (GCS 9-15) the serum level was 73 *u*mol/L and symptoms included drowsiness (80%), ataxia (53%), nystagmus (38%), vomiting (17%), and dystonia (7%). Patients with carbamazepine serum levels greater than 150 *u*mol/L may require intensive life support. (Tibballs J. Acute toxic reaction to carbamazepine: clinical effects and serum concentrations. J Pediatr Aug 1992; 121:295-299.) (Reprints: James Tibballs, MBBS, Intensive Care Unit, Royal Children's Hospital, Flemington Road., Parkville, Victoria, Australia 3052.)

COMMENT. In a study from the University of Cincinnati, Ohio, the administration of activated charcoal resulted in a statistically significant reduction in carbamazepine half-life but the time to complete recovery from overdose was not affected. (Wason S et al. Carbamazepine overdose - the effects of multiple dose activated charcoal. Clin Toxicol March 1992; 30:39-48.) The authors recommend no more than 2 to 3 doses (1 gram per kilogram) of activated charcoal in order to prevent

formation of concretions and continued absorption of the drug. Prolonged repeated use of activated charcoal after carbamazepine overdose in comatose patients is not beneficial and carries a hazard of aspiration.

VALPROATE-INDUCED CEREBRAL EDEMA

A case of cerebral edema resulting from acute sodium valproate poisoning in a 19 year old male is reported from Northwick Park and East Birmingham Hospitals, UK. On admission the patient was unconscious and the plasma valproate concentration was 900 mg/L. He had taken 1200 mg of sodium valproate along with 1500 mg of aspirin. The salicylate blood level was 70 mg/L. CT showed gross cerebral edema with slit-like ventricles and absence of cortical sulci and basal cisterns. Gastric lavage, fluid restriction and IV dexamethasone resulted in slow recovery. Acute complications included liver and renal dysfunction, hypocalcaemia and generalized muscle spasms. (Khoo SH, Leyland MJ. Cerebral edema following acute sodium valproate overdose. Clin Toxicol June 1992; 30:209-214.) (Reprints: Dr. S.H. Khoo, Monsall Hospital, Newton Health, Manchester, M108WR, UK.)

COMMENT. External leakage from feeding gastrostomies was reported in 4 of 8 children who received valproate sprinkle at the Hennepin County Medical Center, Minneapolis, MN (Jones-Saete C et al. Epilepsia July/Aug 1992; 33:692-695). Adherence of undissolved valproate particles to the exterior of the tube appeared to prevent the close approximation of the tube to the gastrostomies stoma. The problem was reduced by changing the tube more frequently or using a larger size tube.

SEIZURE DISORDERS

PYRIDOXINE DEPENDENT EPILEPSY

Four children with pyridoxine dependent seizures beginning at 2 to 19 months are reported from the Loyola University Medical Center, Maywood, IL. Patients were identified out of 51 treated routinely with pyridoxine for refractory seizures and seen over a 6 year period. The dose of pyridoxine was 50 mg orally twice daily. The seizure types were atypical absence, myoclonic, generalized clonic and simple partial and complex partial. The authors suggest that pyridoxine should be tried in all children with seizure disorders with onset at any age who are poorly responsive to anticonvulsant drugs. (Coker SB, Postneonatal vitamin B_6 - dependent epilepsy. Pediatrics Aug 1992; 90:221-223.) (Reprints: S.B. Coker, M.D., Loyola University Medical Center, 2160 S. First Ave., Maywood, IL 60153.)

COMMENT. Pyridoxine dependent epilepsy may present after the neonatal period and may be manifested by many seizure types. Many of us have been discouraged by failure to uncover pyridoxine dependency in drug resistant epilepsies in children. Obviously, persistence rewards, but the relationship between pyridoxine and epilepsy is complex.