Phenytoin

Class: Antiarrhythmic Agent, Class I-B; Anticonvulsant, Hydantoin

Pharmacokinetics

Absorption

i.) Non-genetic
- a. Formulation used
- b. Route of administration
- c. Manufacturer: variable bioavailability
- d. Food: increased absorption
- e. Enteral (tube) feeds: decreased absorption
- f. Antacids: may decrease absorption
- g. Concomitant medications: p-glycoprotein inhibitors

ii.) Genetic
- a. Genetic variation in p-glycoprotein gene

Distribution

i.) Non-genetic
- a. Altered serum protein (88-93% protein bound, primarily to albumin)
- b. Concomitant medication/substances
  - i. Other highly protein-bound drugs can displace phenytoin from protein binding sites
  - ii. P-glycoprotein inhibitors or activators
- c. Uremia: decreased volume of distribution
- d. Age: increased volume of distribution in premature neonates

ii.) Genetic
- a. Genetic variation in p-glycoprotein gene

Metabolism

i.) Non-genetic
- a. Concomitant medications/substances: CYP2C9, CYP2C19 inducers or inhibitors
- b. Hepatic impairment: decreased clearance
- c. Age: decreased metabolism in geriatrics

ii.) Genetic
- a. Genetic variation in drug metabolizing enzyme gene(s): CYP2C9, CYP2C19

Excretion

i.) Non-genetic
- a. Renal impairment: excretion may be decreased

ii.) Genetic
- a. No clear genetic factors affecting excretion

Pharmacodynamics

Receptors

i.) Non-genetic
- a. No clear non-genetic factors affecting receptors

ii.) Genetic
- a. No clear genetic factors affecting receptors

Transporters

i.) Non-genetic
- a. Concomitant medications/substances: p-glycoprotein inhibitors or activators

ii.) Genetic
- a. Genetic variation in p-glycoprotein gene