

phenytoin saturable pharmacokinetics

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Pharmacokinetics, V_d , clearance, first-order, half-life, zero-order, dose-dependent, loading-dose, maintenance-infusion. Volume of distribution V_d . Phenytoin may be given intravenously to patients who cannot receive the drug orally or who require rapid onset of drug effect. The Alcohols Chapter Pharmacodynamic interactions may also occur with other drugs including CNS depressants. Nonlinear kinetics is usually due to saturation occurring in one of the pharmacokinetic mechanisms: Patients with unusually low levels may be non-compliant or hyper-metabolizers of phenytoin. On the other hand, for drugs with saturable absorption or tubular reabsorption, a change in dosage may lead to a less than proportional change in plasma concentration. For monitoring a plasma phenytoin concentration, it is critical to know if the observed level represents a steady state value. This capacity-limited metabolism explains the interindividual variability and the lack of predictability of the phenytoin plasma concentration-time profile, because the maximum capacity varies from patient to patient. For drugs with saturable elimination, an increase in dosage or dosage frequency can lead to a disproportionate increase in plasma drug concentration when the rate of elimination tends to reach its maximum capacity. It may also be used in the prevention of seizures following head trauma, and in ventricular arrhythmias. The plasma half-life for aspirin is approximately 15 minutes; but the half-life for salicylate lengthens as the dose increases. The drug is highly bound to both plasma proteins mostly albumin and to tissue components. Some of these metabolites are further metabolized by conjugation with glucuronic acid. Phenytoin follows nonlinear (or zero-order) kinetics at therapeutic concentrations, because the rate of metabolism is close to the maximum capacity of the enzymes involved. In nonlinear kinetics, clearance and half-life fluctuate with plasma concentration. As the rate of administration increases, the plasma concentration at. Therefore, changing dose is difficult and unpredictable. Special caution should be taken when deciding to change the dosage regimen of such drugs, particularly if elevated plasma concentrations are associated with toxicity (e.g. phenytoin). On the other hand, for drugs with saturable absorption or tubular reabsorption. Chapter 9. Nonlinear Pharmacokinetics: Introduction; Saturable Enzymatic Elimination Processes; Practice Problem; Practice Problem; Drug Elimination by . Saturable metabolism, Phenytoin, salicylic acid, theophylline, valproic acidb Figure shows plasma leveltime curves for a drug that exhibits saturable kinetics. Because phenytoin follows nonlinear or saturable metabolism pharmacokinetics, it is possible to attain excessive drug concentrations much easier than for other compounds that follow linear pharmacokinetics. Clinicians should understand that all patients with toxic phenytoin serum concentrations in the listed ranges. often combined with phenytoin. Displacement will lower the total serum concentration but will little affect the free drug concentration. The metabolism of phenytoin to the major metabolite. 5-(p-hydroxyphenyl)(phenylhy- dantoin. is saturable. giving rise to a non linear dose-serum concentration relationship. Therefore. the. Monitoring phenytoin serum concentrations. Phenytoin is a commonly used anticonvulsant but is one of the most difficult drugs to dose appropriately. It has a narrow therapeutic range and, because of saturable metabolism, small dose increases can result in disproportionately large increases in serum concentrations. phenytoin concentration as the concentration increases to the recommended therapeutic range. n These nonlinear kinetics are also referred to as concentration- dependent, saturable, zero-order, or Michaelis-Menten kinetics. n The half-life is not constant and will increase as the serum concentration increases within and. This type of pharmacokinetic profile has been described as saturable pharmacokinetics, capacity-limited pharmacokinetics, or nonlinear pharmacokinetics. Furthermore, there are large interindividual differences, making dose adjustment challenging, so TDM is particularly useful in phenytoin. The usual therapeutic plasma. Phenytoin. OH. OH. CYP2C9. - Polymorphic. - Interactions. - Saturable. (Male, Age 69). Phenytoin for seizures > phenytoin toxicity. Accused of public drunkenness. Unstable [phenytoin] on 90mg/day (1/. 4. 1/. 3 usual dose). Feb 10, - Two imp causes: I) Capacity - limited metabolism - enzyme &/ cofactor saturation; Phenytoin, Alcohol. II) Enzyme induction - decrease MICHAELIS MENTEN EQUATION The kinetics of capacity limited or saturable processes is best described by Michaelis-Menten equation. $dC/V_{max} \cdot C \cdot I$.