Therapeutic Drug Monitoring (TDM) & Managing Narrow Therapeutic Index (NTI) Drugs

Por Cristiano Ricardo · Publicado em 20/06/2007

University clinical pharmacology treatise by Prof. Cristiano Ricardo on therapeutic drug monitoring (tdm) & managing narrow therapeutic index (nti) drugs (Clinical Pharmacokinetics & Precision Pharmacotherapy), featuring mathematical PK/PD modeling, clinical cases, and colorful schematics.

Versão online e eventuais atualizações:
https://cristianoricardo.com/post/therapeutic-drug-monitoring-tdm-managing-narrow-therapeutic-index-nti-drugs-2007-06-20

Clinical Pharmacokinetics & Precision Pharmacotherapy · Clinical Pharmacology & Pharmacotherapy

Narrow therapeutic index drugs require precise serum concentration assays paired with Bayesian dosing algorithms to prevent catastrophic toxicity while ensuring clinical efficacy.

Pharmacological Mechanism & Kinetic Schema

TOXIC ZONE (Above MTC)

THERAPEUTIC WINDOW (MEC to MTC)

SUB-THERAPEUTIC ZONE (Below MEC)

Steady State reached (4-5 half-lives)

The Steady-State Equilibrium Principle

Upon repeated dosing at constant intervals (tau), drug accumulation occurs until the rate of elimination matches the rate of administration. True steady-state is achieved strictly after 4 to 5 elimination half-lives (t1/2). Serum blood draws executed before steady-state attainment yield dangerously misleading pharmacokinetic interpretations.

Vancomycin AUC/MIC Guided Monitoring

Consensus clinical guidelines have shifted from isolated trough monitoring (15–20 mg/L) to 24-hour area-under-the-curve over minimum inhibitory concentration (AUC24/MIC) targets of 400 to 600 mg·h/L. This approach maximizes bactericidal killing against MRSA while

dramatically reducing the incidence of acute kidney injury (AKI).

Aminoglycoside Extended-Interval (Once-Daily) Dosing

Exploiting concentration-dependent bactericidal killing (Cmax/MIC >= 8–10) and the post-antibiotic effect (PAE), consolidated single-dose regimens achieve high therapeutic bactericidal spikes while allowing extended washout periods where trough levels drop below 1 mg/L, preventing saturable endocytic uptake into renal proximal tubular cells.

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