OPT - PHARMACOKINETIC PARAMETER OPTIMISATION FOR INDIVIDUAL PATIENTS

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The advent of rapid drug assay techniques has demonstrated the necessity for interpretative procedures to allow therapeutic drug monitoring results to be fully utilised. OPT is a package of computer programmes which calculates the most likely set of pharmacokinetic parameter values for individual patients, thus permitting drug dosage to be optimised with regard to any desired therapeutic range.

The one compartment open model is assumed, defined by the four parameters clearance (Cl), volume of distribution (V_d), the first order absorption rate constant (k_a) for oral administration and the estimated plasma concentration at the start of drug monitoring (C_o). Initial estimates for each parameter are obtained by applying existing nomograms which relate to patient information such as sex, weight, smoking habits, alcohol intake and biochemical data reflecting cardiac, respiratory, renal and liver function. Information about the patient's dosage history and the resultant plasma drug concentration measurements are combined to form the objective function (Sheiner et al, 1979, Kelman et al, 1982)

$$L = \sum_{1}^{4}\left(\frac{\theta_i - \bar{\theta}_i}{\sigma_i}\right)^2 + \sum_{1}^{n}\left(\frac{C_j - \hat{C}_j}{\sigma_j}\right)^2$$

where the four parameters (θ) are Cl, V_d, k_a and C_o. The σ_i are the estimated standard deviations of the population parameter distributions; the C_j are the measured plasma concentrations; the $\hat{C}_j$ are the corresponding expected concentrations considering the dosage history; the n is the number of measurements. The most likely set of pharmacokinetic parameter values for the individual patient is calculated by obtaining the set which produced the minimum value of L. The greater the number of concentration measurements, then the greater will be the confidence in the final parameter values which are subsequently used to select the most appropriate dosage regimen.

Thus, using the OPT package data for each patient can be entered, edited, updated, stored, and the most likely set of pharmacokinetic parameter values calculated. Any form of drug administration can be dealt with, as can non steady state data. The range of drugs for which the system is currently available include theophylline, digoxin, disopyramide, lignocaine, gentamicin, phenytoin, valproic acid and procainamide.

OPT can be implemented either on a mini computer or on a microcomputer, and should greatly facilitate the choice of drug dosage requirements for individual patients.

Sheiner et al (1979) Clin. Pharmac. Ther. 26, 294-305.
Kelman et al (1982) "OPT: A package of computer programmes for parameter optimisation in clinical pharmacokinetics." British Journal of Pharmacology(1982) (in press).

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