Integrated pharmacometrics from pharmacodynamic data

Christian Jeleazcov

Anästhesiologische Klinik, Friedrich-Alexander-Universität
Erlangen-Nürnberg, Erlangen, Germany

The relationship between the time course of drug dosing and time course of drug effect is a complex non-linear functional. The concept of pharmacokinetics and pharmacodynamics has imposed a useful structure on this relationship.
This presentation reviews some of the assumptions made in the
mathematical modelling of this relationship and how a clinical view onto this relationship might modify the classical way of parameter estimation.
For nearly all anesthetic drugs the concept of pharmacokinetics and pharmacodynamics decomposes the nonlinear functional into apharmacokinetic functional which can be considered as linear and which incorporates the entire time dependence of the functional and into a pharmacodynamic functional which incoporates the entire non- linearity of the system but which reduces to a mere function between concentration and effect. Traditionally both parts are determined from the simultaneous measurement of dose, concentration and effect.
Given the model structure as identified from the classical phar- macokinetic-pharmacodynamic model identification and parameter estimation procedure one can show that the measurement of concentrations is not necessary for parameter estimation but that in essence the simultaneous measurement of dose and effect is sufficient.
The future development of model based adaptive dosing strategies
could be entirely based on pharmacodynamic measurement, which eventually could lead to a new interpretation of the acronym TCI, whereby the 'Target' is not the target concentration but the target effect.