Poster

[P27-10] P27-10: Pharmacokinetics and pharmacogenetics

Chair: Andrew Somogyi, Australia

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[P27-10-10] Education in clinical pharmacokinetics: clearance and elimination rate constant parameterizations are equally valid

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Background

Unending controversy has existed about parameterizing a pharmacokinetic (PK) model.–Is volume (V) and clearance (Cl) better, or is V and Ke, the rate constant of elimination? Basic PK parameterizations can be V and Cl, V and Ke, or Ke and Cl. Pharmacokinetic education has deduced what happens after a change in volume, etc.. These are treated as important theoretical questions. However, the controversy persists, because among other things there has been no significant effort, and no tools until recently [1], to obtain data from actual unstable patients to obtain definitive answers. Everything has been speculation or deduction, but little based on actual data.

Methods

The Principle of Invariance

(adapted from [2]): If *q* is a maximum likelihood estimate (MLE) of a parameterization of interest *q* which has *p* parameters, and *g(q)* is a function that maps *q* to a new parameterization that has *n* parameters, where *n p*, then *g(q)* is an MLE of *g(q)*. It states that a maximum likelihood estimate (MLE) of a function of a parameter is equal to that function of the original MLE of the parameter itself. If one has a certain data set and estimates a function g of a parameter –or g() - the answer is equal to the function g of the original MLE of itself.

Results

Suppose Bill likes V and Ke, but Alice likes V and Cl. When both analyze the same data set, using MLE, Bill gets estimates V_{Bill} and Ke_{Bill}, while Alice gets estimates V_{Alice} and Cl_{Alice}. The fact is that both Alice and Bill get identical parameter estimates: $V_{Alice} = V_{Bill}$, and $Cl_{Alice} = V_{Bill}$ times Ke_{Bill}.

Conclusions

All three parameterizations –V and Cl, V and Ke, and Ke and Cl, are equally valid. No parameterization is better than any other. This result resolves the controversy concerning the parameterizations.

References:

1. Bayard D, and Jelliffe R: A Bayesian Approach to Tracking Patients having Changing Pharmacokinetic Parameters. J. Pharmacokin. Pharmacodyn. 31 (1): 75-107, 2004.

2. Goodwin G and Payne R: Dynamic System Identification: Experiment Design and Data Analysis. Academic Press, New York, 1977, p 50..