STOCHASTIC DIFFERENTIAL EQUATIONS MODELLING OF LEVODOPA CONCENTRATION IN PATIENTS WITH PARKINSON’S DISEASE

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BACKGROUND

• Westin et al. [1] developed a pharmacokinetic-pharmacodynamics model for duodenal levodopa infusion described by four Ordinary Differential Equations (ODE), the first three of which define the pharmacokinetic model.

OBJECTIVES

• Introduce stochasticity in the pharmacokinetic model of levodopa concentration to check whether inter-individual variability may be separated into measurement noise and system noise.
• Investigate whether the SDE based model provide better fits than the ODE counterpart, by using a real data set.

METHOD – DATA USED

• Pooled from 2 studies investigated by Westin et al. [1]
• First study had 3 patients, who were given bolus dose in the morning. Data was collected for 2 hours on two non-consecutive days.
• Second study had 5 patients with 3 occasions each. Data was collected on the patients for 4 hour-periods with five different infusion rates in 2.5 days.
• Plasma samples were anlyzed by high performance chromatography.

METHOD – MODELLING

• System noise variables are added to the previously developed ODE model through a standard Wiener process (Brownian motion) [2], as shown below.

\[ \frac{da_0}{dt} = Inf - k_a a_0 + \sigma_w dw \]  
\[ \frac{da_1}{dt} = BIO \cdot k_a a_0 - \left( \frac{Q}{V_1} + \frac{CL}{V_1} \right) a_1 + \left( \frac{Q}{V_2} \right) a_2 + \sigma_w dw \]  
\[ \frac{da_2}{dt} = \left( \frac{Q}{V_2} \right) a_1 - \left( \frac{Q}{V_2} \right) a_2 + \sigma_w dw \]

BIO = bioavailability (fraction absorbed); \( \sigma_w \) = system noise.

REFERENCES