Modelling the Effect of Exercise on Insulin Pharmacokinetics in "Continuous Subcutaneous Insulin Infusion" Treated Type 1 Diabetes Patients - DTU Orbit (12/12/2018)

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Introduction: The artificial pancreas is believed to ease the burden of constant management of type 1 diabetes for the patients substantially. An important aspect of the artificial pancreas development is the mathematical models used for control, prediction or simulation. A major challenge to the realization of the artificial pancreas is the effect of exercise on the insulin and plasma glucose dynamics. In this report, we take the first step towards a population model of exercise effects in type 1 diabetes. We focus on the effect on the insulin pharmacokinetics in continuous subcutaneous insulin infusion (CSII) treated patients by modelling the absorption rate as a function of exercise.

Methods: Three models are estimated from 17 data sequences. All of them are based on a linear three-compartment base model. The models are based on stochastic differential equations to allow noise to enter the dynamics. In the first model, the insulin absorption rate parameter is replaced by a random walk. In the second model, the relationship between the absorption rate and exercise is modelled as a linear dependency, while in the third model this linear relationship depends on the intensity. A Lamperti transformation is used to ensure non-negative state values. A special focus is put on the structural identifiability of the base model, while the posterior identifiability is checked for all models from the conditional likelihood profiles.

Results: The first model is disregarded due to the small number of observations during the exercise bout. From likelihood-ratio tests and information criteria, the third model is appointed as the best model to model the relationship between exercise and the insulin absorption. The posterior identifiability check showed that it was not possible to identify the variance of the measurement variance.

Conclusion: A model to predict the insulin appearance in plasma during exercise in CSII treated patients is identified. Further clinical studies are needed to confirm the increase in insulin plasma concentration during exercise in type 1 diabetes patients. These studies should include dense sampling to allow for a fully data driven identification of an appropriate model.