Modeling and Visualization of Integrated Insulin and Glucose Time-Activity Profiles

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Objectives: To establish a pharmacokinetics (PK)-pharmacodynamics (PD) model integrating the relationship of PK associated with various insulin formulations, administered separately or in combination, and the resulting PD impact shown as glucose profiles.

Methods: A population modeling approach implemented via nonlinear mixed effects modeling (NONMEM v7) was utilized to build the PKPD model. The model was validated and qualified by comparing model predictions with clinical observations and was subsequently used to project insulin (PK) and glucose (PD) profiles of common insulin regimens and dosing scenarios. Visual plots of PK and PD profiles for commonly prescribed regimens, such as a rapid-acting insulin (i.e., lispro) alone or in combination with a basal insulin (i.e., glargine), were executed via the R statistical program, while the R package, Shiny (RStudio, Boston, MA), was applied to enable a web-browser interface for interactive execution and viewing of the simulation outputs.

Results: An interactive model was created that includes features, such as the influence of patient characteristics, type of insulin or their combinations, insulin dose, and timing of administration relative to meal consumption.

Conclusions: The analysis demonstrates that traditional modeling and simulation techniques, when utilized in combination with contemporary web applications, can potentially provide dedicated diabetes health care providers with an efficient and intuitive educational tool to visualize the anticipated individualized PK and PD outcomes based on multiple conditions for a variety of insulin regimens in both Type 1 and 2 diabetes patients.