Journal of Diabetes Science and Technology
Volume 2, Issue 4, July 2008

ORIGINAL ARTICLES

A Subcutaneous Insulin Pharmacokinetic Model for Computer Simulation in a Diabetes Decision Support Role: Validation and Simulation

Jason Wong, B.Eng.,[1] J. Geoffrey Chase, Ph.D.,[1] Christopher E. Hann, Ph.D.,[1] Geoffrey M. Shaw, MBChB, FJFICM,[2] Thomas F. Lotz, Dipl. Ing, Ph.D.,[1] Jessica Lin, B.Eng., Ph.D.,[1] and Aaron J. Le Compte, B.Eng.[1]

Abstract

Objective:

The goal of this study was to validate a previously derived and identified physiological subcutaneous (SC) insulin absorption model for computer simulation in a clinical diabetes decision support role using published pharmacokinetic summary measures.

Methods:

Validation was performed using maximal plasma insulin concentration (C_{max}) and time to maximal concentration (t_{max}) pharmacokinetic summary measures. Values were either reported or estimated from 37 pharmacokinetic studies over six modeled insulin types. A validation comparison was made to equivalent pharmacokinetic summary measures calculated from model generated curves fitted to respective plasma insulin concentration data. The validation result was a measure of goodness of fit. Validation for each reported study was classified into one of four cases.

Results:

Of 37 model fits, 22 were validated on both the C_{max} and the t_{max} summary measures. Another 6 model fits were partially validated on one measure only due to lack of reporting on the second measure with errors to reported or estimated ranges of <12%. Another 7 studies could not be validated on either measure because of inadequate reported clinical data. Finally, 2 separate model fits to data from the same study failed the validation with 90 and 71% error on t_{max} only, which was likely caused by protocol-based error. No model fit failed the validation on both measures.

continued →

Author Affiliations: [1]Department of Mechanical Engineering, University of Canterbury, Christchurch, New Zealand, and [2]Department of Intensive Care, Christchurch Hospital, Christchurch School of Medicine and Health Science, University of Otago, Dunedin, New Zealand

Abbreviations: (C_{max}) maximal plasma insulin concentration, (IV) intravenous, (MI) monomeric insulin, (NPH) neutral protamine Hagedorn, (PK) pharmacokinetic, (RI) regular insulin, (SC) subcutaneous, (t_{max}) time to maximal concentration

Keywords: blood glucose, compartmental models, decision support, diabetes, hyperglycemia, insulin, simulation, subcutaneous injection

Corresponding Author: Jason Wong, Department of Mechanical Engineering, University of Canterbury, Private Bag 4800, Christchurch, New Zealand; email address *xww10@student.canterbury.ac.nz*

Abstract cont.

Conclusions:

A previously derived and identified model was clinically validated for six insulin types using C_{max} and t_{max} summary measures from published pharmacokinetic studies. Hence, this article presents a clinically valid model that accounts for multiple nonlinear effects and six different types of SC insulin in a computationally modest form suitable for use in clinical decision support.

J Diabetes Sci Technol 2008;2(4):672-680