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Analysis

Diabetes Simulators: Ready for Prime Time?

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DIABETES IS A DISEASE OF COMPROMISES. Irrefutable evidence demonstrates that good glycemic control significantly reduces the risk for developing many of the devastating long-term complications of diabetes. Conversely, limitations inherent in the current methods for providing insulin replacement make euglycemia a very dangerous proposition for most type 1 diabetics because of the risk of severe hypoglycemia. Normal beta cells within the pancreas modulate insulin secretion, responding in minutes to small changes in blood glucose concentrations. This tight feedback loop maintains blood glucose concentrations within a narrow range. Current clinical insulin regimes pale in comparison.

Patients, and often their families, face a substantial challenge as they tread the narrow path between low- and high-glucose concentrations each day. Using a handful of glucose determinations each day, they must integrate diet and activity with a bewildering array of possible exogenous insulin preparations and doses to forge a reasonable level of glycemic control. Given this complexity, patients and providers alike seek a clear-cut set of rules to guide them to euglycemia. Given our increasing understanding of physiology and the massive computing capability on our desktops, an algorithm to predict glucose concentrations does not seem, at first blush, an unreasonable request. With some patient-specific information, shouldn't we be able to accurately predict the glucose concentrations resulting from various dietary and insulin regimens?

In the article elsewhere in this issue, Dr. E.D. Lehmann discusses one such glucose simulator, *AIDA v4.0.* This program is freely available via the Internet. A DOS program, it ran reasonably well in a Windows 95 environment. The user interface is a bit cumbersome. The program uses a physiology-based, single glucose compartment model to integrate the actions of carbohydrates and exogenous insulin. Glucose enters the compartment by intestinal absorption and liver gluconeogenesis. Glucose leaves the compartment via insulin-independent and insulin-dependent pathways. Hepatic and peripheral glucose utilization are modeled separately so that different insulin sensitivities may be assigned to each. Renal glucose losses occur when the renal threshold is exceeded. Insulin concentrations (from virtual subcutaneous injections) are derived using a two-compartment model. Counterregulatory hormones, exercise, stress, and circadian variations in insulin sensitivity are not included within this model. The technical guide that is included in the program contains a complete description of the equations involved in the model. The author has done some evaluation of the potential clinical utility of this model using patient specific parameters derived from actual historical glucose concentrations. Reasonably large differences were found between predicted and actual glucose concentrations.

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Both the program itself and the article discussing the program repeatedly stress that *AIDA* is not designed to provide patient-specific advice regarding diabetes management but is, rather, strictly an educational tool. The author proposes that this simulator might be helpful in teaching both patients and professionals to control glucose concentrations more effectively. While the author reports some of the feedback he has received regarding this program, the effectiveness of the program to improve glycemic control in either setting has not really been tested.

Features such as occasionally missed insulin doses and random variation in glucose concentrations would improve the clinical realism of the simulation. Finally, improved user interfaces are needed to increase acceptance of simulators as educational tools. Changes in the virtual management regimen must be easy to make and the resulting impact on virtual glucose concentration easy to see and compare. In this regard, computer game-based formats may well be more effective for many patients. As Dr. Lehmann himself states, however, formal trials are essential to demonstrate that this (or other simulators) can actually help improve diabetic management.

Do physiology-based glucose simulators have a role beyond educational aids? The addition of components to the model would increase its complexity and perhaps its ability to predict clinically relevant glucose concentrations accurately in an individual patient. Development of such a model would certainly highlight gaps in our knowledge of the physiology involved in glucose homeostasis, an admirable goal in and of itself. Would random variations, such as in carbohydrate or insulin absorption, preclude glucose predictions accurate enough to guide an individual patient to better control? Absent a practical glucose sensor, are 4 to 8 glucose values per day sufficient to properly "tune" a glucose simulator to an individual patient? I don't know. Clearly some patients with complete insulin deficiency are able to achieve good glycemic control despite all these random variations and with infrequent sampling. Many of these patients, however, seem to use regimens that incorporate more feedback correction than actual simulation of impact of management changes on future glucose concentrations.

Simulators are useful endeavors. Simulators that accurately reflect the real world permit exploration of actions that would be difficult or impossible to perform in the real world. Even imperfect simulators can serve to identify important areas where knowledge is insufficient, pointing the way for further study.

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