A minimal mathematical model for interpretation of data from continuous glucose monitoring

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Introduction

One common application of mathematical biophysics is to build the pharmacokinetic/pharmacodynamic modeling (PKPD), when the change in the concentration of the pharmacological agent (drug) in the body is described by a differential equation, the terms on the right side of which is a function of the rate of assimilation of drugs and elimination from the body. Despite the seeming simplicity in terms of mathematics, PKPD models allow us to make useful predictions about the doses and treatment schemes specific to the patient. The present work is devoted to the construction of a mathematical model (PKPD), describes the glucose homeostasis in humans. The purpose of building this model is the ability to quickly assess the parameters of glucose metabolism in the body of the specific patient's diabetic and hypoglycemic therapy prediction scheme optimal for him.

Aim: is to construct a mathematical model that takes into account the main physiological parameters of blood glucose regulation, in order to identify them for individual patients according to the CGM data.

Materials and Methods

The data of CGM of 6 pregnant women with diabetes mellitus type 1, age 27.2±3.,4 years, 15.3±2.7 weeks of pregnancy. The data of two patents with diabetes mellitus (one with MII and one with CSII) with detailed diary. In diary dose insulin, amount of carbohydrates, physical activity was checked in. The mathematical model consists of six ordinary differential equations, describing dynamics of blood and interstitial glucose level and the hormones and drugs concentration in blood. The model integration and parameter estimation were performed in COPASI software (http://www.copasi.org/).

The mathematical model is a system of differential equations that describe processes, as reflected in the traditional model of the physiological regulation of glucose. The glucose level in the model is determined by the following equation:

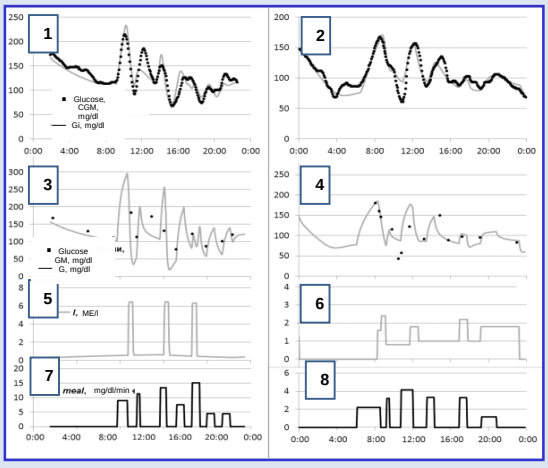
$$\frac{dG}{dt} = -(p_3 - int) \cdot G - p_4 \cdot x \cdot G + ext \cdot G_i + p_5 \cdot N + a \cdot meal,$$

where *G* - the concentration of glucose in the blood, *Gi* - glucose concentration in interstitial fluid, *N* - concentration of contrinsulin factors in the blood, *meal* - glucose level increase as a result of food. The elimination of glucose from the bloodstream insulin independent tissues is proportional to the concentration of glucose in the blood - the proportionality coefficient *p3*. Communication in blood glucose levels with the adoption of the food is quite complicated and there are mathematical models that describe all the processes of glucose uptake in different areas of the gastrointestinal tract and activity of digestive enzymes. However, in this study it is not possible for every patient evaluate all parameters of glucose utilization in the digestive tract, so the model introduced only two parameters describing the absorption of glucose from food. Namely, a constant flow of glucose from the gastrointestinal tract *(meal),* which is determined by the ratio of the amount of consumption of bread units for the duration of digestion, glucose utilization and efficiency ***a.***

Results

The developed model described experimental data well. For patients with type 1 diabetes mellitus generally insulin production was zero and parameters of insulin elimination higher than those for healthy donors. Patient-specific parameters included glucose uptake efficiency and rate of blood-interstitial glucose interconversion. Relative objective value is 3% for the patients with accurate data and 1% for the patients without exactly data.

Picture 1



Description of glucose metabolism parameters in patients using a mathematical model. (1, 3, 5, 7) - 1 patient (2, 4, 6, 8) - Patient 2. (1, 2) - the time dependence of the concentration of glucose in the interstitial fluid space, points are given experimental data obtained by continuous monitoring glucose. (3, 4) - time dependence of the blood glucose concentration data points are specified from their diaries patients. (5,6) - the estimated concentration in the blood of insulin (insulin was modeled on the basis of data from the personal diaries of patients). (7, 8) Receipt of food from the digestive tract (based on individual patients diaries and matching parameters).

Conclusions

The constructed mathematical model could be utilized for assessment of patient-specific parameters from continuous glucose monitoring data. Received a personalized model of the regulation of blood glucose, which can be used to predict the results of CGM according to the modification of the assigned glucose-lowering therapy. One would expect that this approach can significantly reduce the number of iterations of the selection of medical therapies hypoglycemic and therefore increase the effectiveness of treatment according CGM.

References

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