GLOBAL ACADEMIC RESEARCH INSTITUTE

COLOMBO, SRI LANKA

International Journal of Engineering Science (IJES)

ISSN 2424-645X

Volume: 01 | Issue: 01

On 15th January 2019

http://www.research.lk

Author: Eugene O. Podchasov

Bauman Moscow State Technical University, Russia

GARI Publisher | Engineering Science | Volume: 01 | Issue: 01

Article ID: IN/GARI/ICET/2018/112 | Pages: 31-36 (06)

ISSN 2424-645X | Edit: GARI Editorial Team

Received: 23.11.2018 | Publish: 15.01.2019

DEVELOPMENT OF THE ALGORITHM FOR AUTOMATION OF PUMP INSULIN THERAPY

Eugene O. Podchasov

Department of Robotics and Complex Automation, Bauman Moscow State Technical University, Russia

podchasov@bmstu.ru

ABSTRACT

The paper describes a method for monitoring and correcting diabetic glycemia, intended for use in automated closed-loop therapy systems, also called artificial pancreas. The presented algorithms allow to increase the accuracy of the Continuous Glucose Monitoring and to reduce fluctuations of the glycemia and amount of hypo and hyperglycemias. The effectiveness of the application of various control algorithms in the course of adjustments is considered.

Key words: Diabetic glycemia, Closed-loop systems, artificial pancreas, Continuous Glucose Monitoring, fluctuations of the glycemia, control algorithm

INTRODUCTION

The World Health Organization (WHO) calls diabetes mellitus among the four major noncommunicable diseases threatening humanity [1]. According to recent studies, the prevalence of diabetes among people over 18 years of age is 8.5% [2]; Diabetes and its complications, such as kidney failure, heart attacks, strokes and vascular lesions of the limbs, resulted in 3.7 million deaths in 2012.

To reduce the risk of complications of diabetes mellitus, it is necessary to carry out activities aimed at maintaining the glucose concentration in the blood of patients within the recommended values, which can be achieved with the use of different treatment strategies. The most universal type of diabetes therapy is insulin therapy, which consists in the introduction into the body of human insulin or its analogues of different validity. Among the most promising methods of insulin therapy is the automated administration of drugs with the help of insulin pumps.

LITERATURE REVIEW

Modern insulin pumps, in addition to the insulin delivery mechanism, provide the possibility of continuous monitoring of the patient's glucose level, and some of them have the ability to program for the introduction of insulin at variable rates depending on the time of day. The pumps of the latest models, among other things, have systems for preventing hypoglycemia. As a result of the use of such systems, the quality of life of patients can be improved;the continuous introduction of insulin, which simulates the normal functioning of the pancreas, can reduce the fluctuation of glycemia, which leads to a reduction in the incidence of complications [3]. In this paper, the possibility of developing and implementing mathematical algorithms for glycemic control in patients with diabetes mellitus for automated therapy systems is considered in order to improve the quality of their functioning. Most experts in the field of diabetes therapy are of the opinion that therapy with insulin pumps will not achieve reasonable therapeutic and cost-effectiveness at all until the pump acquires "feedback" from the patient's body [4]. In fact, this means that the main goal of developing and improving insulin pumps is to translate their functioning into a "closed cycle", that is, in fact, turning them into artificial pancreas systems.

METHODOLOGY

Let's compare the ratio of the insulin profile of a healthy person to a patient with diabetes mellitus receiving therapy according to the traditional scheme (Figure 1) with a constant level of basal insulin and three boluses (Figure 2)

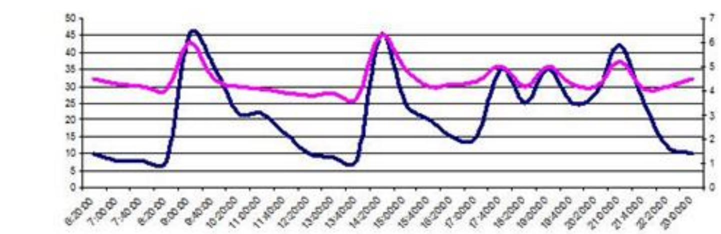
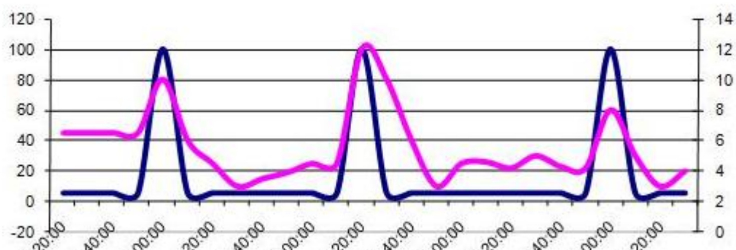


Figure 1. Profile of a healthy person (insulin level is blue, glucose level is purple)



The system should ensure the approximation of the profiles in Fig. 2 to the profiles in Fig. 1,

to model the work of a healthy pancreas.

In view of this requirement for new devices, their structure must necessarily include modules and systems capable of performing the following functions:

•Continuous monitoring of glycemia in real time;

•Control of the rate of basal insulin administration;

•Calculation and administration of bolus insulin;

•Prevention of hypo- and hyperglycemia;

•Change in modes of insulin administration.

Given the specifics of the application of systems, its modules should be implemented in the simplest way to ensure the minimum cost of the system. For this, some of the functions should be performed using integrated modules that combine several purposes. There are developments [5] in the area of differential regulators for calculating and delivering insulin. The regulator used is described here by a function of the form

$$PID(t) = K_p(G - G_t) + K_i\int(G - G_t)dt + K_d\frac{dG}{dt},$$

where G is the measured glycemia at the time t, Gt is the target glycemia, Kp, Ki, Kd are the coefficients for the proportional, integral and differential parts of the regulator, respectively. The presented control gives a positive result on the computer model at the coefficients calculated on blood measurement for venous insulin administration, without taking into account the arising errors. The modification of this algorithm will be considered below.

DATA ANALYSIS

Consider an example of correction of blood glycemia from a single measurement of glycemia of the intercellular fluid of subcutaneous fat, the graphical representation of which is given in Fig. 3. The quantization period of the process is 20 minutes.

The blue curve is the result of measurements of glycemia in the subcutaneous fat tissue, the result of which is used to calculate the correction of insulin therapy. The correction of the insulin level is calculated for the time of 14:00 on the actual values from the blue curve. At the same time, the actual blood glucose level is determined by the pink curve, the lag time is one quantization period (the error is represented by the green region).

The average period of absorption and activation of ultrashort insulin analogs is 20 minutes, that is, one more quantization period (pink area on the graph).

Suppose that adjusting for one dimension is safe and effective. Consider how such an adjustment affects the level of glycemia (fig. 4).

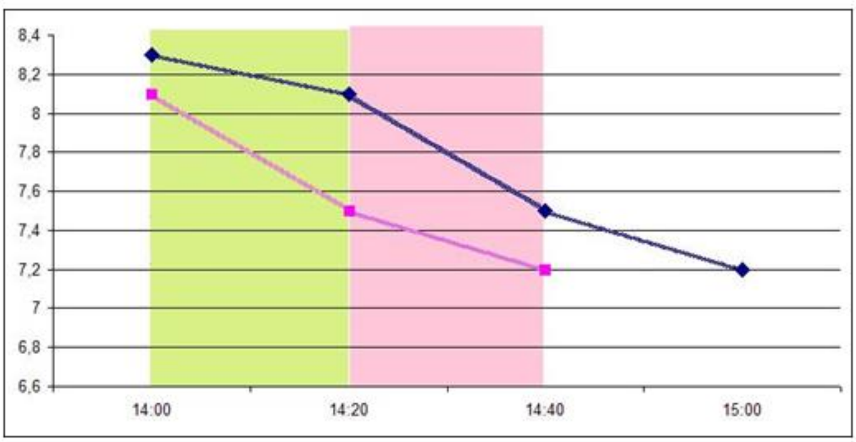


Figure 3. Graphical representation of the single-dimensional adjustment process

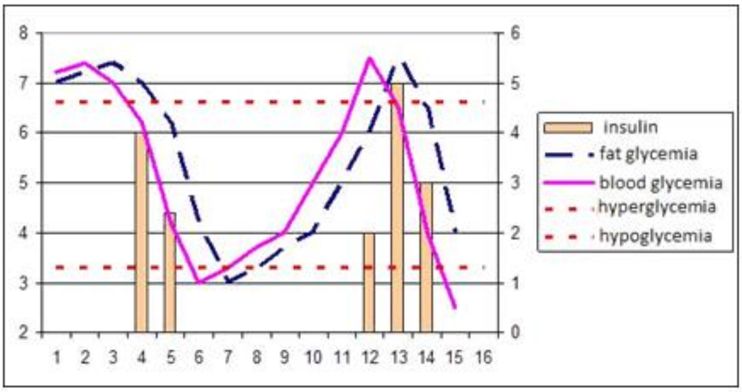


Figure 4. One-value adjustment

Correction of glycemia begins at time 4, the measured value of glycemia in the subcutaneous fat is 7 mmol, the calculated dose of insulin is 4 units. The actual blood glucose level at this time is 6.3 mmol. After absorption and activation of insulin in the next step, the blood glucose level will be 4.2 mmol, in the subcutaneous fat - 6.3.According to the indications of glycemia subcutaneous fat, a correction dose of insulin 2.4 units was calculated. After its introduction and absorption, the level of glycemia drops to 3 mmol, that is, hypoglycemia occurs, which means a process overshoot. Thus, the settlement control is actually applied not to the initial value, but to the next two periods, that is, it lags by two periods, which makes the current value management ineffective.

The rate of insulin administration should be determined based on the calculation of the necessary dose of insulin to reduce the predicted glycemia [6-7]. It is known that in order to lower the blood glucose level to a predetermined value, it is necessary to introduce units of insulin, where I is the required dose of insulin, Gi is the measured glycemia, Gt is the target glycemia, Cf is the factor of insulin effectiveness determined experimentally.

$$I = \frac{G_i - G_t}{C_f}$$

The insulin delivery rate V can then be determined as:

$$V = \frac{\left(\frac{(G_p(n) - G_t(n))}{C_f} - \frac{(G_p(n-1) - G_i(n-1))}{C_f} \right)}{t_c}$$

where V is the rate of administration, unit / hour, $\frac{(G_{\Pi}(n) - G_{\amalg}(n))}{C_f}$ - the necessary volume of insulin to correct the predicted level of glycemia, $\frac{(G_{\Pi}(n-1) - G_{\amalg}(n-1))}{C_f}$ - the amount of "unused" insulin remaining due to the excess of predicted glycemia over the actually measured after the previous correction cycle, t_c - the quantization time of the correction process, usually 20 -30 min.

It is suggested to use a moving average to predicate glycemia through quantization period, and thereby increase accuracy of therapy. The following equations are suggested [8-11]:

1. $k_1 \cdot \overline{G_i}$;
2. $k_1 \cdot \overline{G_{i-1}} + k_2 \cdot (\overline{G_{i-1}} + \overline{G_i})$;
3. $k_1 \cdot \overline{G_{i-1}} + k_2 \cdot (\overline{G_{i-1}} + (\overline{G_i} + k_1 \cdot \overline{G_{i-1}}))$;

Where $\overline{G_i}$ is moving average value on i^{th} step, calculated with 3 last glycemia level; $\overline{G_{i-1}}$ is moving average value on $(i-1)^{th}$ step; $\overline{G_{i-2}}$ is moving average value on $(i-2)^{th}$ step, k_i - correction coefficients.

The results of mathematical modeling of correcting glycemia (fig. 5) with prediction with moving average is shown on fig. 6

measurement, prediction and correction of glycemia.

Computational experiment proved the possibility and effectiveness of the developed algorithm of glycemic control

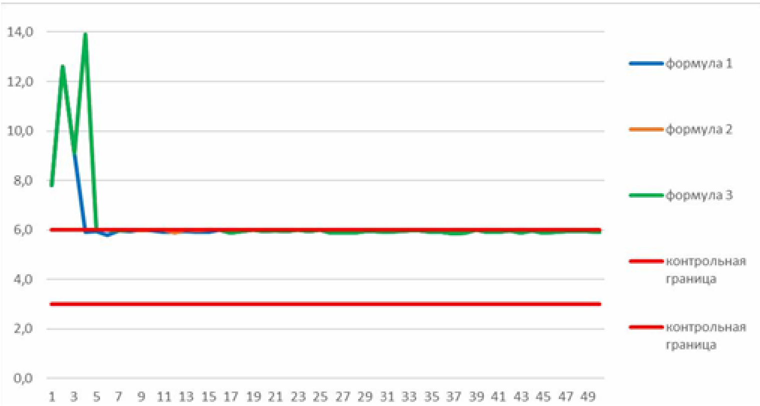


Figure 6. Mathematical model of correction using prediction

DISCUSSION

According to the presented results of the conducted studies, it can be concluded that the introduction of corrections in the control of glucose concentration as a whole gives a positive effect and allows you to meet the control limits.

CONCLUSION

The conducted researches allowed to draw the following conclusions:

Existing glycemic control systems can not function as an "artificial pancreas" system.

The developed control algorithm for the automated pump allows to approximate the results of its work to the operation of the pancreas.

The programmed statistical module allows to increase the accuracy of and allowed to identify the most effective control functions.

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