Development of Failure Model for Reliability Increment of Automated Mechatronical Insulin Pumps

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***Abstract*—The increment of reliability of automated insulin pump is important for development of effective ways for diabetes treatment. Existing models of automated insulin pump don't allow to use them in closed-loops regime, as their probability of failure is too high. This paper deals with development of generalized model of automated system failures. For that purpose division of automated system for 4 basic blocks with specific conditions of failures is proposed. The cases of failures are analyzed and generalized. The model for system reliability is proposed.**

***Index Terms*— Automated pump, reliability, failure**

I. 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 die 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 [3].

Among the most promising methods of insulin therapy is the automated administration of drugs with the help of insulin pumps. Some of the existing insulin pumps may include system for prediction glucose level in patients' blood and control block for therapy clarification, which means that it may be used in so-called closed-loop regime, as artificial pancreases. However, the automated closed-loop regime is almost never used beyond testing and medical experiments, as the reliability of such systems is still insufficient [4-6].

This problems means, that there is a high demands in development of new schemes and constructions of the insulin pumps and the ways for its.

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An insulin pump is a medical device intended for continuous administration of doses of ultra-short-acting insulin analogue of an insulin analogue to a patient with diabetes [4]. A traditional insulin pump consists of a pump itself, which is a device for delivering a drug, consisting of a power source, an insulin pump and a power source, a replaceable container with the drug, and an infusion set representing a subcutaneous injection system and connecting tubes [5].

Insulin pumps, like the pancreas of a healthy person, inject insulin in two complementary ways. Basal administration of insulin allows you to simulate the pancreatic secretion of insulin in the background, in response to the production of glucose by the liver from the glycogen stored in it. Basal administration occurs continuously throughout the day. The bolus administration of insulin with a pump simulates an increased release of insulin in response to food intake [6].

The pancreas of a healthy person secretes insulin with a variable speed, depending on stress, physical activity, and the level of other hormones. The pump injects insulin at low speeds and in small volumes. The administration of basal insulin can be programmed in a predetermined mode, so that the rate of administration of insulin will depend on the time of day.

Modern insulin pumps can be equipped with glycemic measurement systems. Such systems can both be integrated into pump and tick mechanisms and exist as separate measuring sensors that can be connected to the pump.

Depending on the version, the measuring system can either take measurements at the request of the patient, or operate in a continuous glycemic monitoring mode. In turn, continuous monitoring of glycemia can be carried out either in the "blind" mode, or in the "real time" (NMH-RV) [7].

Glycemia control in the "blind" mode, also called "professional monitoring", consists in continuous recording for the purpose of further retrospective analysis, and information about the measurement results is not transmitted to the patient and is not used in calculating the pump operation parameters. When working in real time, the measurement system allows you to get graphs of changes in the level of glycemia over time, as well as signals to the patient about

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the glycemia indicators beyond the established target values.

The additional use of the real-time daily glycemic monitoring system and the correct analysis of the curve on the instrument display prevents the development of hyper- and hypoglycemic conditions and, thus, does not cause an increase in the daily need for insulin. The sensor works on the same principle as the test strips for the glucometer - using a specific enzyme - glucose oxidase. [8] In this case, the device (pump) directly obtains information on the signal strength that arises during the reaction of the enzyme applied to the sensor and glucose in the intercellular fluid of subcutaneous adipose tissue. A pump (or other device for continuous measurement of glycemia) compares the signal strength values with the glycemia indicators that the patient receives as a result of self-monitoring using a glucometer (the comparison process is called calibration). At the same time, calibration should be carried out only 2-3 times a day, and the pump displays the glycemia indicator continuously for many days.

In clinical practice in Russia, models of automated pumps manufactured in the USA, Switzerland and Korea are used; pumps from AccuChek (Roche), Medtronic, are presented in online stores

DANA Diabecare pump is available (there is no representative office in Russia) [7, 9].

Figure 1. Insulin pump Medtronic Paradigm MMT 715

The simplest insulin pump - Medtronic Paradigm MMT 715 (Fig. 1), has a Russian-language menu, the function of an assistant bolus.

Figure 2. AccuChek Combo insulin pump

AccuChek Combo (Fig. 2) - in addition to the pump, there is a remote glucometer that allows you to remotely calculate a bolus, measure blood sugar and give the pump a command to administer insulin.

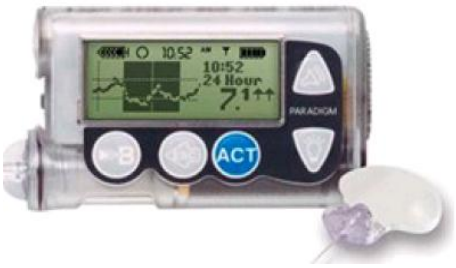

Figure 3. Medtronic Paradigm MMT 722 insulin pump

Medtronic Paradigm MMT 722 - in addition to the capabilities of MMT 715, it has the function of continuous monitoring of blood glucose in real time (NMH-RV). Data can be viewed on the pump screen and analyzed using a computer using special software.

Figure 4. Medtronic Paradigm Veo MMT 754 Insulin Pump

Medtronic Paradigm Veo MMT 754 - has all the functions of MMT 722, is the only pump that can stop the administration of insulin if low blood sugar is detected with constant monitoring of glucose.

Based on the review, the following conclusions can be drawn:

1) insulin pumps used in Russian practice do not have a sufficiently large memory;

2) it is proposed to interact with the pump using a personal computer using special software;

3) of the six used models of insulin pumps, only three are capable of autonomously controlling glycemia to some extent, of which only two US production models have the function of continuous monitoring of NMH-RV;

4) the Medtronic Paradigm Veo MMT 754 pump has the greatest degree of automation, and the control is to turn off the pump in case of hypoglycemia.

This suggests the need for work in the field of automation of the processes of functioning of insulin pumps [10].

II. Automated System Structure

The artificial pancreases is the system, consisting of interconnected electro-mechanical and biological parts, which should work together to achieve a result of correcting glycemic level [7].

III. Basic Parts of Electro-mechanical System

The system of automated glycemic control should include the following modules:

Measuring module: designed to measure the glucose level in a patient's physiological fluid at each time point Must have the foncnbn of continuous glycemic control.

Most often, continuous diagnostic systems use measuring sensors that are installed in the patient's subcutaneous fatty tissue and measure the concentration of glucose in the intercellular fluid.

Calculation and software module: designed to calculate the required rate of introduction of basal insulin and the volume of boluses for ready-made, pre-selected algorithms. Receives information about the measurement of blood glucose from the measuring module.

Given the specifics of the application of the systems, its modules should be implemented in the simplest way to ensure the minimum cost of the system. For this, part of the functions should be performed using integrated modules combining several purposes.

Most experts in the treatment of diabetes mellitus agree that therapy with insulin pumps does not achieve reasonable therapeutically and cost-effectiveness until the pump acquires a “feedback” from the patient's body. In fact, this means that the main goal of the development and improvement of insulin pumps is to transfer their functioning to a "closed cycle", that is, in fact, to turn them into artificial pancreatic systems.

Let us compare the ratio of the insulin glycemic profile of a healthy person and a patient with diabetes mellitus receiving therapy according to the traditional scheme (Fig. 5) with a constant level of basal insulin and three boluses (Fig. 6)

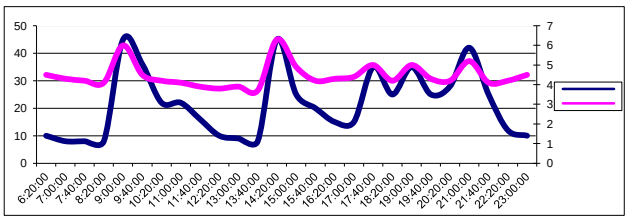

Figure 5. Healthy person profile

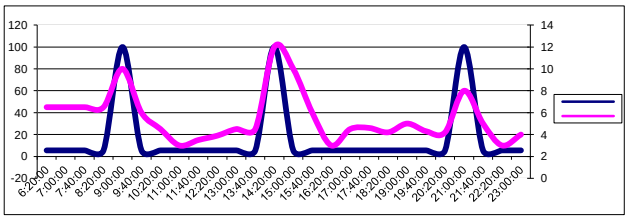

Figure 6. Profile of the patient receiving insulin according to the traditional scheme

The system should ensure the approximation of profiles from Fig. 5 to profiles 6, i.e. simulate the work of a healthy pancreas.

Given such a 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;
- Management of the rate of administration of basal insulin;
- Calculation and administration of bolus insulin;
- Prevention of hypo- and hyperglycemia;
- Changing the regimen of insulin administration.

Given the specifics of the application of the systems, its modules should be implemented in the simplest way to ensure the minimum cost of the system. For this, part of the functions should be performed using integrated modules combining several purposes.

There are developments in the field of proportional-integral-differential regulators for the calculation and delivery of insulin. The regulator used is described by a function of the form

$$PID(t) = K_P(G - G_G) + K_i \int (G - G_G)\,dt + K_D \frac{dG}{dt}$$

where G is the measured glycemia at time t, G_G is the target glycemia, K_p, K_i, K_D are the coefficients for the proportional, integral, and differential parts of the regulator, respectively.

A diagram of a feedback control system of this kind is presented in Fig. 7

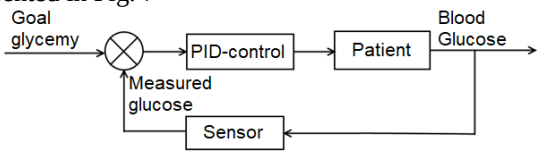

Figure 7. Feedback management

The presented control gives a positive result on a computer model with coefficients calculated on a blood measurement during venous administration of insulin, without taking into account the errors that arise. Modification of this algorithm will be considered later.

Accumulative module: it is intended for storing data on glycemic levels intended to control the course of the disease by the attending physician, as well as information about the therapy carried out to correct the algorithms.

Corrective-teaching statistical module: designed to develop control algorithms for insulin administration and their periodic adjustment This module can be implemented in the form of a computer program associated with the settlement and software and cumulative modules.

The module of insulin administration intended for direct injection into the body of patients [8-12].

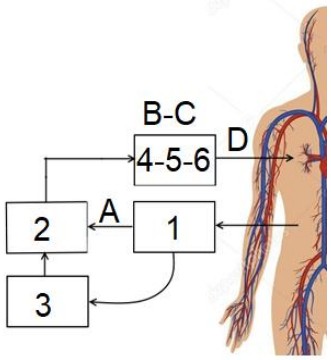

Figure 8. Structural diagram of automated system

During the operation of the system, the measuring sensor 1, installed in the patient's subcutaneous fat, performs continuous monitoring of the patient's glucose level. The measurement results are transmitted via communication channel A to software and computing

module 2. Software and computing module 2 conducts continuous data exchange with the training and correction module, which compares the latest glucose measurements with previous predictions, and corrects the selected algorithm for calculating the rate of insulin administration. Information about the parameters of the insulin administration process and glucose levels in the subcutaneous fat is stored in the cumulative module 3 [13-14].

After adjusting the calculation algorithm, the computational software module calculates the prediction of the glycemic level and, according to it, corrects the rate of insulin administration. The calculated speed is converted into a control signal for the pump motor 4.

The rotor of the electric motor insulin pump 4 as a result of the flow of control comes into rotation. Its angular velocity is determined, on the one hand, by the incoming action, and on the other hand, by the dynamics of the mechanical drive. Given that the nominal speed of rotation of the pump links is small, a change in the kinetic energy of the pump due to the variability of the external forces will lead to a significant fluctuation of the angular velocity of the engine.

Movement from the engine is transmitted using a gear pair 5 connected to the output shaft B of the engine and the input shaft C of the screw pump 6. In order to reduce the mass of the structure directly carried by the patient, the elements of modules 4 and 5 are made of polymeric materials.

Modules 4, 5, and 6 together form the insulin administration module.

The insulin injection module is associated with the patient's body through a catheter D, which is connected to the cannula E, which is installed in the subcutaneous fat.

Let us consider an example of correction of blood glycemia by a single measurement of glycemia of the intercellular fluid of subcutaneous fat, a graphical representation of which is given in Fig. 9. The quantization period of the process is 20 minutes.

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

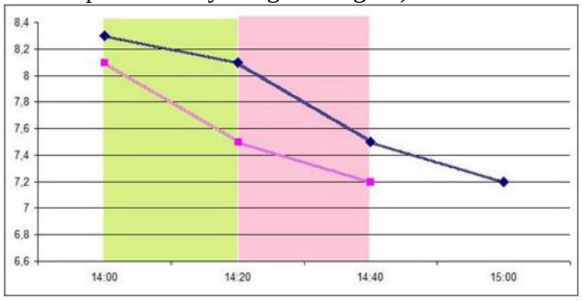

Figure 9. Graphical representation of the unit-based adjustment process

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

Assume that one-dimensional adjustment is safe and effective. Consider how this adjustment affects the level of glycemia.

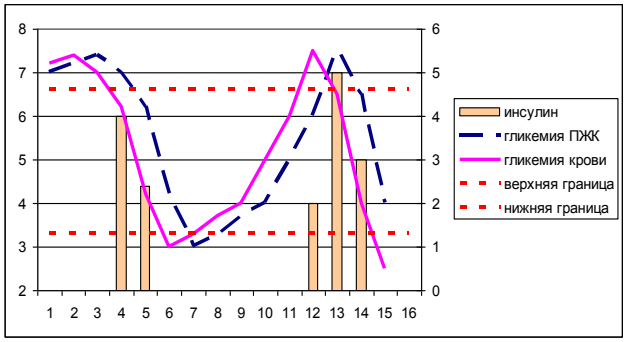

Figure 10. Single value adjustment

The 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 level of blood glycemia at a given time is 6.3 mmol. After absorption and activation of insulin in the next step, the level of glucose in the blood will be 4.2 mmol, in the subcutaneous fat - 6.3. According to the indications of glycemia of subcutaneous fat, a corrective insulin dose of 2.4 units was calculated. After its introduction and absorption, the level of glycemia drops to 3 mmol, that is, hypoglycemia occurs, which means overshooting of the process.

Thus, the calculated control is actually applied not to the initial value, but to the next one after two periods, that is, it is delayed by two periods, which makes the control by the current value ineffective.

IV. Characteristics of Insulin Pump Failure with Automatic Insulin Injection

The system of continuous administration of insulin should be considered as bioelectromechanical, therefore, its refusals may have a dual nature. On the one hand, system failures are caused by direct failure of the elements of the electromechanical part of the device. An example of such a failure can be damage to the catheter due to mechanical stress on it. On the other hand, the most important in importance is the functional failure of the system, which is the ineffectiveness of therapy with the help of automatic insulin delivery, that is, the patient's glucose level goes beyond the control values.

Conducted clinical studies of the use of the developed system revealed 28 cases of side effects [14]. Among them, 82% of cases of side effects are directly related to glycemia (Fig. 11.)

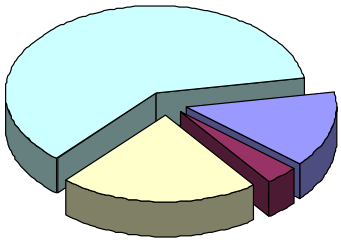

Figure 11. Side effects of insulinoteration according to the scheme of a closed cycle

Among the main sources of strong hyperglycemia when using Medtronic MiniMed 670G pumps in closed-loop mode, the following are highlighted (Fig. 12):

- Mechanical damage of infusion set,
- Software disruptions,
- Malfunctions of the sensor.

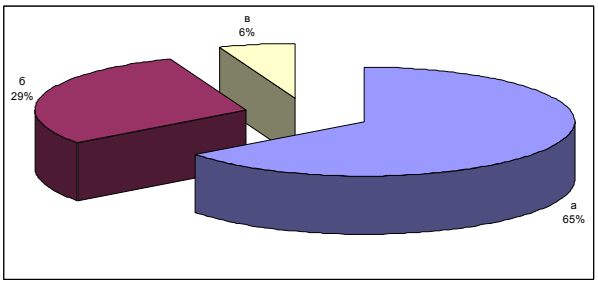

Figure 12. Causes of Strong Hyperglycemia

Some clinical studies [15] also show the need for additional non-systemic administration of insulin in order to improve the quality of treatment (that is, the transition to a semi-closed system).

At the same time, researchers agree that the main reason for inaccuracies in the work of the system is the imperfection of the system for measuring glycemia and the calculation of insulin administration adjustments.

Based on the fact that almost 30% of system failures are caused by mechanical reasons, the design of automated insulin injection systems requires further development, taking into account its reliability.

Failures of the electromechanical part of the drive can be caused by the following reasons:

1. Mechanical damage to the elements when interacting with the external environment

2. Distortion of system dynamics due to changes in external loads

3. Errors of the system and control algorithms

Mechanical damage is most characteristic of a catheter located in the external environment. For him, such types of failures are possible as rupture, detachment from the cannula, and "collapse", characterized by a sharp decrease in the radius of curvature of the midline, leading to the closure of the section.

Distortion dynamics is the most common problem. The reasons for the distortion of the dynamism of the system are associated with changes in the kinetic energy of the system. On the one hand, the kinetic energy of the system changes due to the displacement of the links and the oscillations of their reduced moment of inertia. On the other hand, a change in the shape of a free-hanging catheter leads to a change in the dynamics of insulin flow through it, which, in turn, leads to a change in the load on the pump and a fluctuation in the angular velocity of the engine. In addition, the generalized speed of the system is dependent on the total kinetic energy of the system, which is determined not only by the engine, but also by the movement of the entire system in space with the person. All these factors lead to the fact that the final rate of insulin intake differs from the nominal one, due to which the treatment conditions are violated.

The rate of insulin administration in the basal regimen can be determined based on the calculation of the required dose of insulin to reduce the predicted glycemia. It is known that to reduce the level of glucose in the blood to a predetermined value, it is necessary to introduce units of insulin, where I is the required dose of insulin, G_i and is the measured glycemia, G_{ts} is the target glycemia, C_f is the factor of the effectiveness of insulin, determined experimentally.

The rate V of insulin administration can then be defined as

where V is the rate of administration, units / hour, is the required amount of insulin to correct the predicted glycemic level, is the amount of "unused" insulin remaining due to the excess of the predicted glycemia over the actually measured after the previous correction cycle, the quantization time of the correction process, usually 20 -30 min.

Glycemia is predicted using a moving average [15-19].

Based on the well-known studies and classical mathematical models, several formulas can be proposed by which adjustments could be made when calculating the required amount of the drug to maintain the concentration of glucose in the blood:

1. $k_1 \cdot \overline{G_i}$;
2. $k_1 \cdot \overline{G_{i-1}} + k_2 \cdot \left(\overline{G_{i-1}} + \overline{G_i}\right)$;
3. $k_1 \cdot \overline{G_{i-1}} + k_2 \cdot \left(\overline{G_{i-1}} + \left(\overline{G_i} + k_1 \cdot \overline{G_{i-1}}\right)\right)$
4. $k_1 \cdot \left(\overline{G_i} - \overline{G_{i-1}}\right)$;
5. $k_1 \cdot \overline{G_{i-2}} + k_2 \cdot \left(\overline{G_{i-2}} - \overline{x_{i-1}}\right) + k_3 \cdot \left(\overline{G_i} - \overline{G_{i-1}} - \overline{G_{i-2}}\right)$
6. $k_1 \cdot \left(\overline{G_i} - \overline{x_{i-1}}\right) + k_2 \cdot \left(\overline{G_i} - \overline{G_{i-1}}\right)^2$;
7. $k_1 \cdot \left(\overline{G_i} - \overline{G_{i-1}}\right) + k_2 \cdot \left(\overline{G_i} - \overline{G_{i-1}}\right)^2 + k_3 \cdot \left(\overline{G_i} - \overline{G_{i-1}}\right)^3$

Different prediction formulas have different efficiencies for certain types of fluctuations in glycemia. If the nature of the change in glucose level changes its dependence (for example, the patient's lifestyle changes from passive to active, which leads to large nominal fluctuations) without changing the control algorithm, this can lead to incorrect calculation of the dose of the drug and, as a result, impaired therapy, as shown according to the results of the mat. modeling in fig 13.

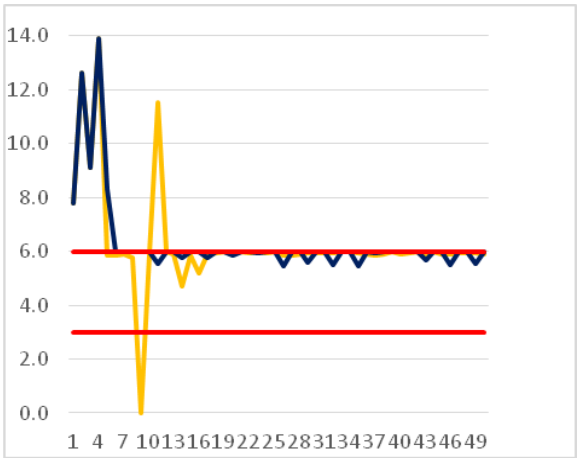

Figure 13. Cases of failure of automated control algorithm 4&5

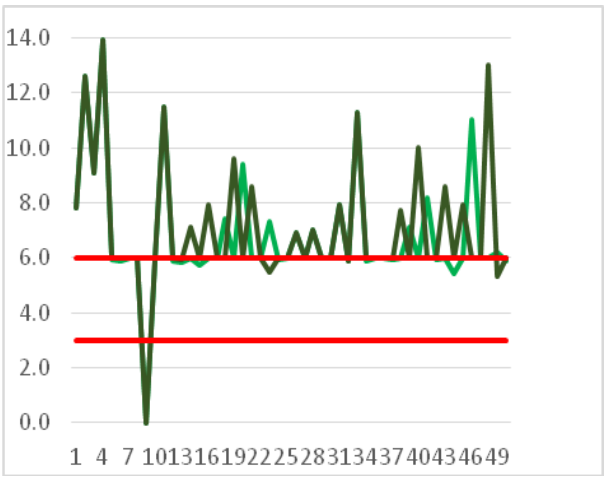

Figure 14. Cases of failure of automated control algorithm 6&7

The overall reliability of the system can be described by the following dependency:

$$P(t) = (1 - Q_1)\left(1 - Q_{4-5-6}^{dyn}\right)\left(1 - Q_A^{mech}\right)(1 - Q_2^{control})$$

Where P is the probability of system failure-free operation, Q_1 is the probability of a sensor failure depending on the time of its service, Q_{4-5-6}^{dyn} is the probability of distortion of the pump dynamics, determined by the design of the insulin administration unit, and also associated with wear and tear service, through the behavior of the catheter with the patient's dynamics and through the hydrodynamic resistance of the subcutaneous fat with the patient's condition, Q_A^{mech}- the probability of damage to the infusion set, related to external conditions and patient activity, $Q_2^{control}$ - the probability of erroneous work management systems associated with a selected set of algorithms and patient characteristics.

To additionally increase the reliability of system, it is needed to estimate the properties of flexible elements. It may be done using the theory described in [20-21].

Conflict of Interest

Author declare no conflict of interest.

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