по шкале MMSE у всех пациентов на 1 сутки показатель был ниже на 20,3%, на 7 сутки на 16,45%, на 30 сутки - 12,3%.

Показатели теста рисования часов у всех пациентов на 1 сутки исследования были снижены на 13,5%, на 7 сутки - на 9,3%, на 30 сутки - 3,8% по сравнению с дооперационной периодом. Соответственно на 17,0 %, 13,0 %, 7,7 % относительно максимально возможного результата.

По шкале FAB у всех пациентов на 1 сутки исследования были снижены на 11,6%, на 7 сутки - на 6,4%, на 30 сутки - на 2,4% по сравнению с дооперационной периодом и относительно максимально возможного результата на 1 сутки - на 18,3%, на 7 сутки - на 13,5%, на 30 сутки - на 9,8% .

По методу А.Р. Лурия у всех пациентов на 1 сутки исследования были снижены на 14,7 %, на 7 сутки - на 7,1%, на 30 сутки - на 2,9% по сравнению с дооперационной периодом. Относительно максимально возможного результата значение теста А.Р. Лурия были на 1 сутки - на 33,0%, на 7 сутки - на 27,0%, на 30 сутки - на 23,7% .

По результатам таблиц Шульте во всех пациентов на 1 сутки исследования были снижены на 36,2%, на 7 сутки - на 26,6 %, на 30 сутки - на 8,6% по сравнению с дооперационной периодом. Относительно максимально возможного результата на 1 сутки - на 43,8%, на 7 сутки - на 33,6%, на 30 сутки - на 14, 6% .

Выводы.

Результаты нашего исследования указывают на наличие когнитивных изменений после операции с использованием общей анестезии. Главным критерием надо выбрать расчет показателя общего когнитивного дефицита. Динамика послеоперационных когнитивных изменений имеет различную структуру и зависит от возраста пациентов, имеет разную динамику восстановления. Общую картину послеоперационных изменений дает их изучения относительно дооперационного состояния и относительно максимально возможного результата по каждой шкале.

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DETECTION GLUCOSE VARIABILITY IN PATIENTS WITH TYPE 2 DIABETES MELLITUS

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ИЗУЧЕНИЕ ВАРИАБЕЛЬНОСТИ ГЛИКЕМИИ У ПАЦИЕНТОВ С САХАРНЫМ ДИАБЕТОМ 2 ТИПА

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Abstract
The experience of using the continuous glucose monitoring system (CGMS) in patients with diabetes mellitus type 2 (DM type 2) is presented in this article. This study helped to identify the both hyperglycemia and hypoglycemia episodes. The patients were about 30 % of the total study time in hyperglycemia and about 8 % in hypoglycemia, including asymptomatic hypoglycemia. The frequency of hypoglycemic conditions depends on the disease's duration and glycosylated hemoglobin (HbA1c) level. CGMS allows carrying out individual, more accurate correction of glucose-lowering therapy.

Аннотация
В статье представлен опыт использования системы длительного мониторирования глюкозы у пациентов с сахарным диабетом 2 типа. Данное исследование позволило выявить эпизоды гипергликемии, в которой пациенты находились около 30 % всего времени исследования, диагностировать гипогликемические эпизоды, которые составляли около 8 % времени исследования, в том числе бессимптомные гипогликемии. Частота гипогликемических состояний нарастала с увеличением длительности заболевания, при снижении уровня гликозилированного гемоглобина. Система длительного мониторирования глюкозы позволяет проводить индивидуальную, более точную коррекцию сахароснижающей терапии.

Keywords: diabetes mellitus, continuous glucose monitoring system, hypoglycaemia, glycosylated hemoglobin.
Ключевые слова: сахарный диабет, система длительного мониторирования глюкозы, гипогликемия, гликозилированный гемоглобин.

The achievement of diabetes control is the priority treatment goal of patients with diabetes i.e. persistent compensation ensures the prevention of diabetes chronic complications. The United Kingdom Prospective Diabetes Study (UKPDS) showed that reducing HbA1c by 1% in patients with DM type 2 is accompanied by decreasing of the premature death risk by 21 %. The risk of microvascular complications is reduced by 37%, the risk of myocardial infarction is reduced by 14% [6, 9]. At the same time, the incidence of hypoglycemic conditions increases with the achievement of normoglycemia. It is known that hypoglycemia can have disastrous consequences such as myocardial infarction, stroke, tachyarrhythmia and sudden death [5, 10]. Patients' overweight, cognitive impairment, dementia are remote consequences of hypoglycemia [1, 2]. Therefore, the target level of HbA1c should be achieved with the minimal risk of hypoglycemic conditions. 7-point blood glucose measurements do not allow to capture the glycemia oscillations at night, asymptomatic hypoglycemia, episodes of postprandial hyperglycemia, which is the independent risk factor of chronic complications [3,4]. That is why there is need for more detailed studies of glycemia during the day in patients with diabetes.

The purpose of the study was to identify glucose variability in patients with DM type 2 with using CGMS to identify the hyperglycemia and hypoglycemia episodes.

Materials and methods

At the Endocrinology Department 63 patients were examined with DM type 2 ranging in age from 48 to 65 years. They filled the ADA questionnaire aimed at diagnosis of hypoglycemic conditions "Low Blood Sugar Questionnaire" (version in Russian, 2013). With the help of the questionnaire a group of patients were identified, presumably having the hypoglycemic state. Those patients were examined with CGMS of the company Medtronic Mini Med, USA.

CGMS had been carried out for 120 hours (5 days), simultaneously self-monitoring of blood glucose was performed by individual glucometer at least 4 times a day. Based on the data CGMS the time was analyzed which patients spent in the range of normoglycemia (3.9 to 10.0 mmol/l), hyperglycemia (more than 10.0 mmol/l) and hypoglycemia (less than 3.9 mmol/l). The number and duration of hypoglycemic condition, the average daily value of glycemia, glycemic fluctuations amplitude, the low blood glucose index (LBGI), high blood glucose index (HBGI) were determined too [7,8].

LBGI >4.5 indicated a high risk of hypoglycemia, LBGI <2.5 – on a low risk of hypoglycemia. HBGI >9 displayed the high risk of hyperglycemia, HBGI <4.5 – low risk of hyperglycemia. The level of HbA1c was studied.

Statistical processing of material was carried out using the program "Microsoft Excel 2013" and the program BioStat.

Results. According to the questionnaire, the risk of hypoglycemia was observed in 27 (42,9 %) patients, these patients underwent CGMS. It was established by CGMS that 25 (39,7 %) patients had confirmed hypoglycaemia.

The patients' characteristic data are shown in table 1

Table 1

Characteristics of examined patients

Index	Patients examined with CGMS, n=27
Age, years	56,6 ±1,01
Sex Female Male	 15 12
Duration DM, years	11,7±1,3
HbA1C, %	8,19±0,09
Range of euglycemia, %	63
Range of hyperglycemia, %	30
Range of hypoglycemia, %	8
Number of symptomatic hypoglycemia	6,2±0,63
Number of asymptomatic hypoglycemia	2,48±0,42

According to the results CGMS, patients were on average 63 % of the time in euglycemic range and about 30 % of the time in hyperglycemic range. Tendency to morning hyperglycemia was revealed in 16 (59 %) patients, postprandial hyperglycemia was observed in 18 (67 %) patients, nocturnal hyperglycemia was revealed in 10 (37 %) patients. The results CGMS are evidence of patients being in the hypoglycemia range on average 8 % of time. The average number of hypoglycemia for 5 days was 6.2±0,63, while asymptomatic hypoglycemia – 2,48±0,42. Severe hypoglycemia (less than 2.8 mmol/l) was not identified.

Analyzing the distribution of hypoglycemic episodes during the day showed that the hypoglycemic condition was observed during the daytime in 20 (80 %) patients, 6 (24 %) patients were recorded nocturnal hypoglycemia. The frequency of hypoglycemic episodes increased with the duration of diabetes (Fig. 1).

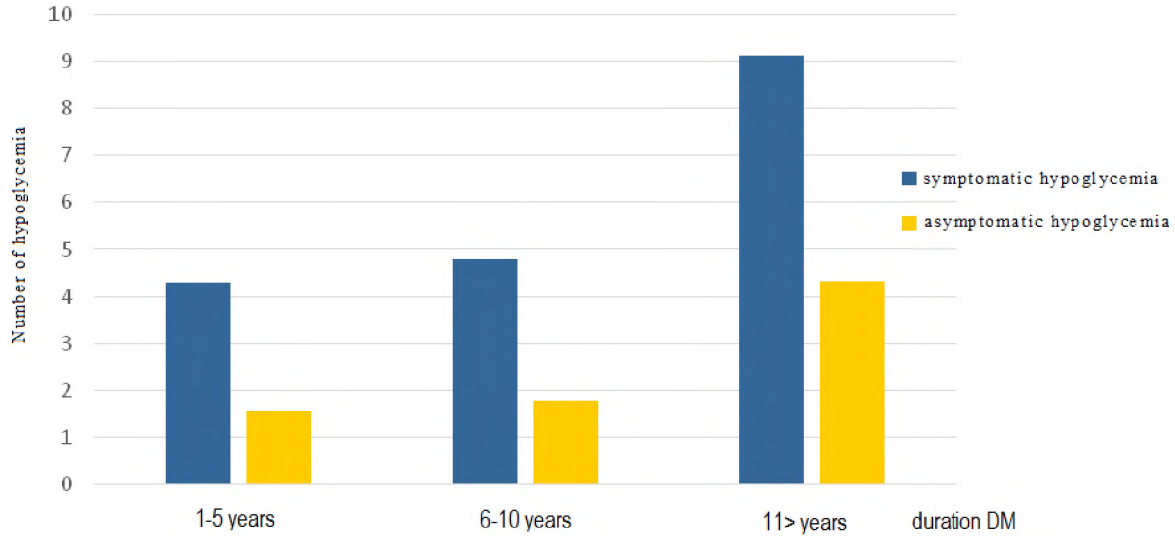

Fig. 1. Dependence of the hypoglycemia frequency on the diabetes duration.

The direct correlation between the diabetes duration and number of hypoglycemia (r=0.53, p=0.04) and between disease duration and the number of asymptomatic hypoglycemia (r=0.75, p=0.07) were established. It suggests impaired regulatory mechanisms of the autonomic nervous system in patients with long diabetes mellitus duration. The number of hypoglycemic conditions increased with a decrease in the HbA1c level, which is confirmed by the presence of a negative correlation (r = -0.73, p = 0.001).

The patients were divided into 3 groups depending on the type of glucose-lowering therapy. The first group included 8 patients receiving the combination of sulfonylurea – glimepiride (doses from 2 to 4 mg once a day) and Metformin (in daily doses from 1700 to 2000 mg). The second group consisted of 9 patients receiving NPH basal insulin (mean dose of 0,15±0,02 U/kg) in combination with Metformin (in daily doses from 1700 to 2000 mg). The third group included 8 patients receiving NPH basal insulin (average dose 0,14±0,02 U/kg) in combination with glimepiride (daily doses from 2 to 4 mg).

Table 2

Patients' characteristics depending on the glucose-lowering therapy

Index	Patients' groups		
	1-st, n=8	2-nd, n=9	3-rd, n=8
Age, years	57,75±1,89	52,22±1,34	54,25±2,08
Duration of DM, years	8,13±1,38	10,11±2,03	9,38±1,02
HbA1C, %	8,34±0,15	8,22±0,17	8,46±0,19
Average daily value of glycemia, mmol/l	9,15±0,49	9,25±0,6	9,22±0,68
LBGI	2,19±0,65	2,62±0,73	6,52±1,47
HBGI	13,61±2,11	9,73±1,56	12,54±2,16

Patients of the examined groups were comparable in levels of HbA1c, age, and the disease duration. The high risk of hypoglycemic conditions development (LBGI 6.52±1,47), and high risk of hyperglycemia (HBGI 12,54±2,16) were found in patients of the 3-rd group treated with combination of basal insulin with glimepiride, these data suggest that carbohydrate metabolism decompensation is probably due to post-hypoglycemic hyperglycaemia.

Patients taking the combination of basal insulin and Metformin, as well as patients using only oral medication (Metformin and glimepiride) had the high risk of hyperglycemia (respectively HBGI 9,73±1,56 and 13,61±2,11). The obtained results indicate the low effectiveness of glucose-lowering therapy in these groups and the need for its intensification.

Clinical case.

A 61-year old women complains of excessive sweating episodes, palpitations occurred after lunch and at night.

From the anamnesis: she has been suffering from diabetes type 2 for 11 years. She was treated by combined therapy – glimepiride 3 mg/day and NPH insulin 14 units in the morning, 12 units in the evening previous three years. When she taking Metformin at a dose of 2000 mg/day effects gastrointestinal dyspepsia were observed, that was why Metformin was discontinued.

Patient is on hypocaloric diet - 1200 kcal/day, she does moderate exercises 150 minutes per week. She performs self-monitoring of blood glucose – 2-3 times a day about 3 times a week.

Clinical diagnosis: Diabetes mellitus type 2, uncontrolled. Steatohepatosis. Diabetic sensory-motor neuropathy. Diabetic nonproliferative retinopathy.

Arterial hypertension II stage, 2 degree, LVH, risk IV. NYHA I.

Obesity 2 degree.

Additional tests: the level of fasting glycemia ranged from 9 to 13 mmol/l, postprandial glycemia is 8-16 mmol/l, HbA1c is 8.5 %.

Objectively: height is 172 cm, weight is 114 kg, BMI of 38.5 kg/m^2. The skin is moderately dry and normal color. The heart rhythm is correct, the tones are muffled, heart rate – 86 beats/min, BP – 160/90 mmHg. The abdomen is soft, moderately painful in the right hypochondrium, the liver protrudes 2 cm under the edge of costal arc. There is no peripheral edema. Pathology of the respiratory system and the urinary tract is not revealed.

For the precise study of glycemic parameters and therapy correction the patient had been undergone CGMS for 5 days. In parallel self-monitoring of blood glucose was carried out.

According to CGMS, only 32% research time the patient spent in a state of normoglycemia, 64 % of the time – in the condition of hyperglycemia, 4 % of the time – in the hypoglycemia condition. For 5 days daily hypoglycemia condition from 1 to 3 in a day was observed, just 5 days 11 hypoglycemic episodes were lasting from 4 to 36 minutes. Four episodes were asymptomatic (3 night and 1 day hypoglycemia). It is important to note that asymptomatic hypoglycemia was often observed at night and it was not determined by conventional methods of self-control. The maximum blood glucose level was 18.3 mmol/l, the minimum is 2.9 mmol/l, the average level of blood glucose - 9.7 mmol/l, and the glycemic fluctuations – 15.4 mmol/l (Fig. 2).

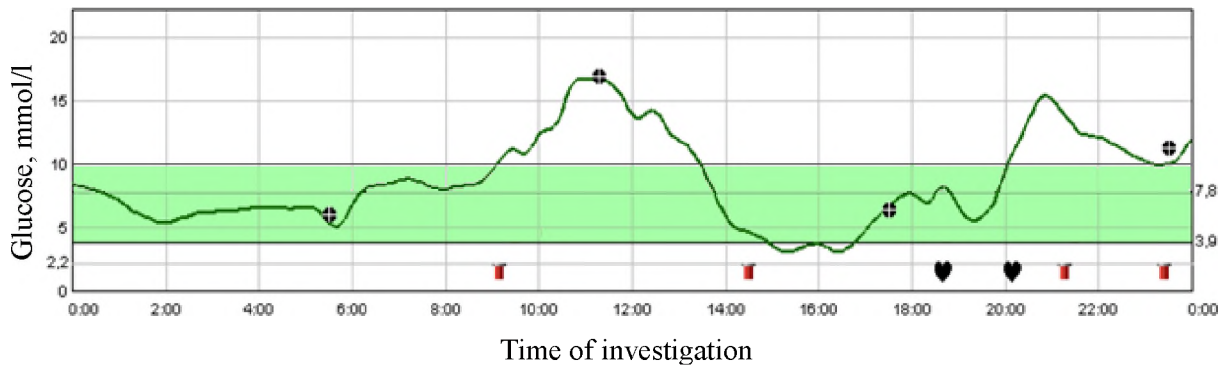

Fig. 2. Initial data of patient's CGMS.

On the CGMS results basis correction therapy was made, NPH-insulin is replaced with basal insulin

Glargine in dose 20 units per day. Glimepiride was discontinued, Glucophage XR (metformin XR) was prescribed at a dose 1000 mg once a day in the evening. Dapagliflozin 10 mg per day was added.

Three months after treatment correction the patient was re-executed CGMS for 5 days. It showed significant improvement in glycemic parameters, 78% research time the patient spent in normoglycemia, 22% of time in hyperglycemia, hypoglycemia was not. The maximum level of blood glucose was 12.4 mmol/l, the minimum level was 5.3 mmol/l, the average level of blood glucose was 7.4 mmol/l, and the glycemic fluctuations – 7.1 mmol/l (Fig. 3) The glycosylated hemoglobin level decreased by 0.7 % and amounted to 7.8 %. Weight loss of 4 kg was observed during the treatment period.

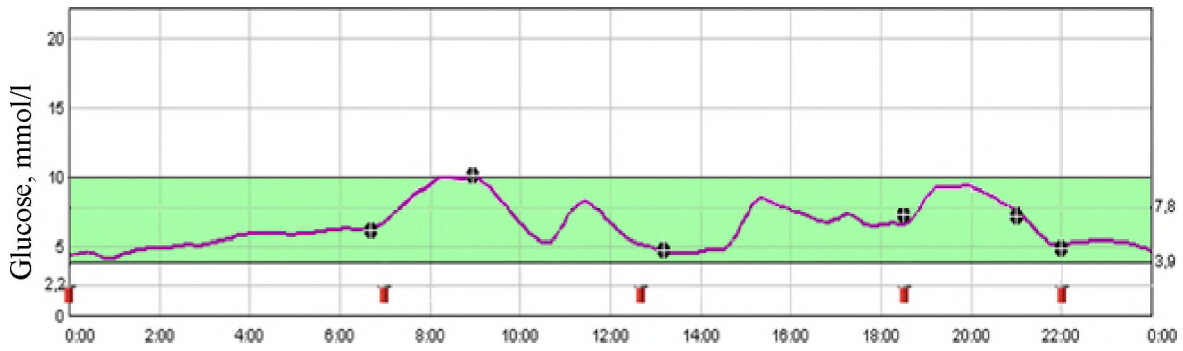

Fig 3. CGMS data after therapy correction.

Conclusions.

The continuous glucose monitoring system provides information on the carbohydrate metabolism uncontrolled state exact causes, namely hyperglycemia and hypoglycemia times. Treatment modification on the base of continuous glucose monitoring system helps to decrease the time of hyperglycemia and hypoglycemia. Elimination of hypoglycemia will reduce the risk of cardiovascular events.

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