To the Question of Carbohydrate Metabolic Disturbance in Women During Pregnancy.

Mary Burduli, Professor of OGASH Academy. Senior Researcher of MPISRL named after Dr. Ernst Theodor Rippmann. General consultant to Outpatient clinical Department named after Rrof. Michael Peikrishvili, Georgia OGASH. Tbilisi, Georgia.
Avtandil Chkheidze, OGASH Chairman and President, Tbilisi State University, Tbilisi, Georgia.

Gestational diabetes mellitus (GDM) – is a carbohydrate metabolic disturbance, which is revealed for the first time during pregnancy. In spite of the fact that pregnancy is a physiological condition it is during that period that carbohydrate disturbances are aggravated due to the result of insulin resistance.
The insulin resistance (IR) begins activating during the second trimester of pregnancy, when placenta produces hormones (cortisol, placental lactogen, estrogens) preserving pregnancy and blocking action of insulin – the "counter-insulin" effect, and which becomes apparent between 20-24 weeks of pregnancy till the 35^{th} week when the grow of placenta stops.

If the carbohydrate disturbance is developing in the second or the third trimester of pregnancy and returns to norm after childbirth (in majority of cases), the threat of potential diabetes mellitus (of type 2) in mother remains due to preservation of insulin resistance after the childbirth.

According to the epidemiological investigations in the USA, GDM develops in approximately 4% of cases of pregnancy. According to the European researches the spread of GDM varies between 1-14%, depending on the population of women. Approximately in 50% of women with GDM, after the childbirth, various carbohydrate metabolic disturbances are stated as a rule after the next 5 and more years. Half of the disturbances are diabetes mellitus of type 2.

If the diagnose of carbonhydrate metabolic disturbance is established in the first trimester of pregnancy then it is a diabetes mellitus which existed before pregnancy but was not diagnosed. Spread of the unstated diabetes among expectant mothers is 0.3%.

It is a well known fact that essential changes of metabolism take place during pregnancy. (See Table 1)

Physiological changes of metabolism in women during pregnancy.

Table 1

Type of metabolism	Glycemia	Character of changes	Origin

Carbohydrate metabolism	**a) 4,0 – 5,2 mmol/l on an empty stomach** **b) ≤6,7 mmol/l postprandial glycemia**	**a) glycemia level decrease on an empty stomach (not 0,5 – 1,0 mmol/l)** **b) Glycemia level increase 2 hours later after meal.**	**Accelerated secretion of glucose by kidneys.** **Decrease of production of glucose by liver.** **Increased consumption of glucose in the system: mother – placenta – fetus.** **The climax of rapid absorption of carbohydrate and bradyperistalsis of gastrointestinal tract.**
Albumin exchange		**Reduction of the quantity of amino – acids circulating in blood.**	**Increase consumption of amino-acids in the system: mother – placenta – fetus.**
Fat exchange		**Increased decay of fat-acids causing formation of keton bodies.** **Increase in fat tissue.**	**Decrease of production of glucose by liver, shortage of carbohydrates in nutrition.** **Increased formation of pregnancy hormones depending on the period of pregnancy.** **Increase in food rich in calories and decrease of motional activity.**

The above Table shows that in pregnant women glycemia on an empty stomach makes up 4.0 – 5.2 mmol/l, postprandial glycemia (two hours later) is not more than 6.7 mmol/l, it means that the fluctuation of glycemia during a day is not so high due to the adequate insulin supply to the organism. GDM is developing if the pancreas fails to cope with the increased load caused by activation of placenta hormones. At the same time, at the second half of pregnancy the level of mother's diabetogenic hormones (ACTH, CTH, cortisol and others) is increasing, the physical activity of a pregnant woman is decreasing, caloric content of food is increasing and gain in weight is observed. This means that the above-mentioned factors make IR active and aggravate carbohydrate metabolism. If an expectant woman with GDM diagnose has hyperglycemia then a hyperinsulinemia is developing in the fetus (on the 13^{th} week of pregnancy, pancreas of the fetus is producing its own insulin). The above mentioned factors lead to diabetic fetopathy and increased risk of development of late pregnancy toxicosis with an expectant mother.

For effective prophylaxis of the above-mentioned complications it is necessary maintain glycemia within norm.

Increased level of glycemia on an empty stomach to over 5.2 mmol/l and to over 6.7 mmol/l two hours after the meal is considered as hyperglycemia and needs adequate correction. If glycemia on an empty stomach is 5,3 mmol/l and two hours after the meal 6.8 mmol/l; or glycemia on an empty stomach is between 4.9 – 6.0 mmol/l then the additional examination is needed for more accurate GDM diagnosis.

GDM Risk Factors

It is well known that genetic predisposition to GDM is realized by the influence of certain risk factors.

For identification of GDM, WHO offered the following criteria of selection of expectant mothers:

- Age over 30 years;
- Disturbance of glucose tolerance in anamnesis;

- Large fetus in anamnesis (4kg and over);
- Casually revealed previous increase level of glucose on an empty stomach or after the meal;
- Some ethnic groups (noneuropean race).

The American Diabetic Association (ADA) offered not to examine the women, who have the following criteria:

- Age less than 25;
- Normal body mass;
- Absence of diabetes of type 2 in relatives;
- Relationship with European race;
- Absence of typical obstetric complications of pregnancy and delivery in anamnesis;
- Absence of GDM in anamnesis.

The risk factors of GDM are as follows:

- Excess body mass, obesity, metabolic syndrome;
- Diabetes mellitus in the relatives of the first relation degree;
- Age over 25 years;
- Disturbance of glucose tolerance in anamnesis;
- Burdened obstetric anamnesis:

- Previous baby with the weight over 4 kg, with big abdominal circumference and the wide shoulder girdle;
- GDM in previous pregnancy;
- Chronic noncarrying of pregnancy (over 3 spontaneous abortions in I or II trimester of pregnancy);
- Hydramnions;
- Stillbirth;
- Defects of development in previous children.

It is established that 40% of women have one or several risk factors of development of GDM. It is recommended that such expectant women should

undergo the glucose tolerant tests with 75g of glucose over the period between 24th-28th week of pregnancy.

Rules of glucose loading:

1. Three days before glucose loading an expectant woman is on the ordinary diet and physical activity.
2. The loading is made in the morning on an empty stomach after 8-14 hours of night starvation.
3. After blood taking on an empty stomach one must drink a glass of glucose containing 75g of dry glucose dissolved in 250-300ml of water.
4. Repeated glycemia is made 2 hours after taking the glucose solution.

The glucose loading is considered positive when:

a) Fingertip glycemia on an empty stomach ≥ 6,1 mmol/l
b) Intravenous glycemia on an empty stomach ≥ 7,0 mmol/l
c) Fingertip or intravenous glycemia after 2 hours of glucose loading ≥ 7,8 mmol/l

In case the results of the glucose loading meet the norms, the repeated loading is made on the 24–28 weeks of pregnancy (when the level of pregnancy hormones is increasing).

During the early term of pregnancy, hyperglycemia cannot be often revealed and when making the diagnosis after 28 weeks it is not always possible to prevent the development of complications with the fetus.

There is information about glucose loading with 50g of glucose. For this 50g of glucose is taken irrespective of time of the day or the last meal. The level of glucose is determined on an empty stomach and after an hour of glucose intake. An hour later, if the level of glycemia is or exceeds 7,8 mmol/l, the glucose loading is considered as positive and there is a need to make a thorough diagnostic glucose loading with 75g of glucose.

It is desirable that all women should undergo a screening test with the 50g glucose load on the 24–28 weeks of pregnancy (women with moderate or high risk

of development of GDM should undergo the screening when consulting for the first time).

The group with moderate risk of GDM includes:

- Women with excess weight;
- Women who during previous pregnancies had:

- Hydramnion;

- macrosomia (4kg and more);

- stillbirth;

- Women gaining body weight during the pregnancy;
- Women aged over 30;

The group of high risk:

- Women with excess weight whose near relations have diabetes type 2;
- Women with disturbed glucose tolerance;
- Women who had GDM during previous pregnancy;

The above-mentioned glucose loadings make it possible to reveal, treat and to prevent the disturbed carbohydrate metabolism in time. For stabilization of normoglycemia, of great importance is a dietary regimen, following the rules and conditions needed for maintenance of normoglycemia. Along with this not only normoglycemia but also the complex analysis of laboratory and instrumental methods of examination, within the normal parameters, allow to determine the normal process of pregnancy.

The following parameters of self-control are of great importance:

- Self-control of glycemia;
- Self-control of ketonuria;
- Self-control of the weight;
- Self-control of blood pressure (BP).

1. Self-control of glycemia

During pregnancy, with the diagnose of GDM, criteria compensation of glycemia are as follows: on an empty stomach less than 5,2 mmol/l; an hour after the meal less than 7,8 mmol/l; 2 hours after the meal less than 6,7 mmol/l;

It is recommended to test glycemia on an empty stomach, before meal, before bedtime, 2 hours after the meal. In case of necessity, to do it at night and during the daytime when ill-being.

Such frequent identification of glycemia is conditioned by the strict criteria of glycemia throughout the pregnancy. It is desirable to keep a diary for self control of the above mentioned parameters.

One must remember, that both the mean level of glucose (<4,8 mmol/l) in blood during day and level of glycemia (>12,0-13,0 mmol/l) cause negative affect on the development of fetus.

It is desirable to investigate the index of fructozamine and HbAIc in the dynamics. The norm of fructozamine index is 235-285 mkml/l, and HbAIc <5,8%.

2. Self-control of ketonuria

Reasons of ketonuria are the following:

a) Glycemia >12,0-13,0 mmol/l.
b) Inadequate quantity of consumed carbohydrates
c) Low-calorie diet
d) Long physical activity.

Chronic ketonuria during pregnancy has a negative affect on the development of nervous system of fetus and intellectual potential of future child. To establish the amount of keton bodies in urine, the special keton test-strips are used. A test strip is put into a test-tube with urine for some seconds. If there are keton bodies test – strip changes its color.

3. Self control of blood pressure (BP)

Arterial hypertension is dangerous for carrying of a pregnancy. Blood pressure of an expectant woman should be taken in the habitual home environment on an empty stomach or 1-2 hours after the meal (against the background of daily physical activity). The top limit of the norm BP is 130/85mm Hg. Fluctuation of arterial pressure within 20 mm Hg is admissible.

4. Weight self-control

Weight should be controlled once a week in the morning on an empty stomach, without clothes, after emptying the bowel and the bladder. Gain in weight has an individual character and depends on the constitution, quality of food before and during pregnancy, and on the number of previous pregnancies. For women with normal body weight the following norms of gaining the weight are recommended: I trimester – 0,6 kg in a month, II trimester 0, 35 – 0,4 kg a week, III trimester 0,3 – 0,35 kg a week.

For the women with deficient body weight:

I trimester – 0,8 kg a month,

II trimester – 0,6 kg a week,

III trimester – 0,5 kg a week.

For the women with overweight body:

I trimester – 0,3kg a month,

II trimester – 0,3 kg a week,

III trimester – 0,2 kg a week.

Considerable gain in weight has a negative affect on the health of mother and child. 30-35 calories a day are needed for one kilo of the ideal body weight of the expectant woman. Daily calories for stout expectant mothers are less than 1800 kilocalorie and following the principles of balanced nutrition. It should be taken into account that an expectant mother should not go without food, as during starvation and the deficit of carbohydrates in the organism the intracellular fat and albumins decay forming keton bodies which freely penetrate through placenta and cause negative affect on the development of fetus.

Thus the considered factors and parameters, to a certain extent, represent interdependent information about the state of carbohydrate metabolism with the women with the risk of development of GDM.

Our motto is: healthy children and mothers – without complications.

References:

1. Nathan D.M Davidson Mb. De Fronzo R.A, Hiene RJ, Henry RR, Pratley R, Zinman B.
American Diabetes Association.
Impaired Fasting Glucose And Impaired Glucose Tolerance. Diabetes Care, 2007; 30:753 - 759.
2. Cryer's P.E: Comment on Nathan D.M, Buse J.B. Davidson M.B et al.
Management of Hyperglycemia In Type 2 Diabetes: Of Therapy. A Consensus Statement From The American Diabetes Association And The European Association For The Study of Diabetes. Diabetologia, 2006, 49: 1711 – 1721, 222.
3. Milewiecz A, Jedrzejuk D, Clinical Aspects Of Obesity In The Gynecological Endocrinologicaly Practice. Maturitas, 2007, 56: 113 – 121.
4. Takamura T, Shimizu A, Ando M, Kaneco S: Comment on: Nathan DM, Buse JB, Davidson MB, et al. Management Of Hyperglycemia In Type 2 Diabetes: A Consensus Algorithm For The Initiation And Adjustment Of Therapy. Diabetologia 2006: 49: 1711-1721, 229.
5. Gilbert. Valais M, Koren G. Pregnancy Outcome After First Trimester Exposure To Metformin: A Meto – Analysis. Fertil Steril; 2006; 86: 658 – 663.
6. T. Trukhina. Gestational Diabetes Melitus. Diabetes and Way of Life, 2003, 3: 5 – 8.
7. Aventis, Gestational Diabetes Melitus . Dianovosti, 2001, 6:16.
8. Briggs GG. Freeman RK. Yaff SJ.
Drugs in Pregnancy and Lactation. Philadelphia PA: Lippincott Williams and Wilkins, 2002.
9. Pallardo F, Herrany L. el al.
Early Postpartum Metabolis Assessment In Women With Prior Gestational diabetes. Diabetes Care, 1999, 22/7: 1053 – 8.
10. Alberti K.G.
The Clinical Implications Of Impaired Glucose Tolerance.
Diabetic Medicine, 1996, 13/II: 927 – 37.

Mail to: burduli-mery@rambler.ru

27.03.2010