Biochemical Markers of Metabolic Syndrome in Pregnant Women

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Abstract

The aim of the study was to elucidate the state of lipid metabolism, the processes of lipid peroxidation (LPO) and the state of the antioxidant system (AOS) in pregnant women with metabolic syndrome. A comprehensive examination of pregnant women without pathology was performed, with signs of a metabolic syndrome. Analysis of the data showed that in pregnant women with impaired glucose metabolism, activation of LPO processes takes place against the background of a decrease in the activity of AOS enzymes. Active metabolites of oxygen (AMC) and LPO products lead to a decrease in the NO content of the main vasodilating factor. As a result of these disorders, hypoxia develops, which significantly affects the formation of the fetus. The data obtained make it possible to recommend the determination of the parameters of the POL-AOS system and the NO-forming endothelial function as additional laboratory tests in pregnant women with metabolic syndrome (MS).

Keywords: Pregnancy; LPO; Antioxidant system; Nitric oxide; Metabolic syndrome

Introduction

Physiological pregnancy is a stress test for β-cells of the pancreas and is characterized by the development of oxidative stress (OS), which is one of the central mechanisms of adaptation to new conditions of vital activity of the body.

In the chain of metabolic and functional-morphological disorders in the metabolic syndrome (MS), the first link is hyperglycemia, which has a direct glucose-toxic effect on tissues and organs, including glycation of cellular and tissue structures. Along with this hyperglycemia induces autoimmune reactions, for example, the formation of antibodies to GAD-65 and enhanced TNF synthesis [1]. In addition, reduced glucose utilization causes deficiency of energy substrates in cells, which disrupts the function of ATP-dependent K+ - Na+ -Ca2+ pumps [2-5]. The complex of metabolic and hormonal disorders is a risk factor for clinical manifestations of pathology of internal organs, including cardiovascular diseases, as well as nephropathy, retinopathy, etc. [6].

The disturbance of lipid metabolism in obesity is accompanied by hyper-triaciglycerolemia, hypercholesterolemia and induction of oxidative stress and development of vascular dysfunction. Moreover, a high frequency of lipid peroxidation intensification is due to the fact that physiological pregnancy is accompanied by such features of carbohydrate metabolism, which in many respects resemble the model of diabetes mellitus. In particular, during gestation, a number of mechanisms are being developed, aimed at slowing the utilization of glucose by the mother’s organism with the goal of uniform and sufficient intake of it to the fetus. First of all, it is a blocking effect on the mother’s insulin hormones of the placenta, the presence of antibodies to the receptors, a decrease in the activity of enzymes involved in the metabolism of glucose. As a consequence, insulin resistance is formed, i.e. Decrease in the biological response of tissues to insulin with compensatory hyperinsulinemia [7,8].

The clinical manifestations of obesity during pregnancy are characterized by the risk of induced premature birth, the need for a cesarean section [9,10], a high risk of a number of postoperative complications such as bleeding, deep vein thrombosis, and the development of infectious complications. At the same time, the presence of obesity is associated with a higher risk of complications in natural childbirth [11-13]. As noted earlier, the presence of obesity during pregnancy increases the risk of perinatal mortality and fetal pathology. The relationship between obesity and the development of fetal macrosomia has long been established [14].

Thus, obesity is associated with such metabolic disorders as insulin resistance, hyperlipidemia, increased activity of inflammation factors, vascular dysfunction. Undoubtedly, these factors can adversely affect the developing fetoplacental complex. Due to the fact that the placenta regulates the flow of nutrients from the mother to the fetus, its condition is a determining factor in the development of obstetric complications. It was revealed that placental abnormalities are associated with fetal growth anomalies, preeclampsia, premature birth, stillbirth [15]. Diseases associated with MS, obesity, diabetes mellitus increase the risk of obstetric complications [16-18], the development mechanisms of which have not been fully studied. However, it has been suggested that an increase in glucose in the blood and a violation of its metabolism in the cells of the organs in pregnant women with MS may be the cause of the formation of ROS and the intensification of LPO processes that play a pathogenetic role [20,21].

Materials and Methods

A complex examination of 24 pregnant women was performed, 14 of which made up the 1st control group (healthy pregnant women), 10 pregnant women - the 2nd group (patients with signs of metabolic syndrome). The examination was carried out in the third trimester of
pregnancy. In view of the lack of Russian standards in determining the body mass index (BMI), we were guided by the recommendations of the US Institute (2009): BMI from 18.5 kg/m² to 30 18.5 kg/m².

Conditions for inclusion of patients in the study were single-pregnancy, age over 18 years, no indication of diabetes mellitus and severe somatic pathology, regular dispensary observation during pregnancy. Exclusion criteria are abortion until 37 weeks, presence of acute infectious pathology, specific infection and sexually transmitted infections.

Criteria for the inclusion of patients in the study groups: The 1st group (control group) - physiological pregnancy, completed with childbirth on time, absence of extragenital diseases and obstetric complications; 2nd group (pregnant women with MS) – BMI 18.5 kg/m², absence of signs of gestosis and placental insufficiency, hypertension before pregnancy 140/90 mmHg. Dyslipidemia-hypercholesterolemia and a decrease in the concentration of HDL.

After the formation of the sample, standard clinical and laboratory methods were used and the lipid profile of the blood was additionally assessed according to total cholesterol, HDL cholesterol, LDL cholesterol, TAG, glucose, glycosated Hb, renal function (microalbuminuria, glucosuria, creatinine, Urea).

The severity of lipid peroxidation was assessed by the content of malonic dialdehyde (MDA) in blood [22]. In addition, the activity of catalase, superoxide dismutase - SOD [23], the concentration of ceruloplasmin [24], the content of total metabolites of nitric oxide - NO were determined in the blood. The statistical processing of the results was carried out using the Microsoft Excel 2007 program. The results are presented as mean and mean error (SEM). The statistical significance of the differences was verified using Student's t-test. The level of statistical significance was considered to be p<0.05.

Results and Discussion

Data analysis showed an increase in blood glucose level in pregnant women with MS from 5.06 ± 0.1 to 5.82 ± 0.19 mmol/l (p<0.01) (Table 1). At the same time, glycated hemoglobin tends to increase from 5.3 ± 0.18 to 5.61 ± 0.18% (p>0.05). Glucosuria was observed in 10% of women. The study of urine glucose is a relatively informative indicator, since the threshold for excretion of glucose in pregnant women is even substantially lowered in norm. Glucosuria in pregnant women with MS is explained by an increase in the glucose reabsorption threshold in the proximal part of the renal tubules and can be considered as a method of protecting the fetus from possible hyperglycemia against the background of the existing insulin resistance. Nevertheless, there are data that glucosuria is accompanied by a large number of complications of pregnancy. Such a manifestation can be the frequency of abortion, reaching 25%, macrosomia of the fetus, which is detected 5 times more often than in the population. Therefore, in all cases it is necessary to identify the causes of glucosuria [25].

A significant decrease in the excretion of creatinine in the urine testifies to a violation of the nitrogen excretory function of the kidneys, as evidenced by an increase in its serum level of up to 93.6 ± 0.14, with a control of 88.14 ± 0.12 μmol/l (p<0.01) (Table 1).

Simultaneously, there is a decrease in the concentration of the total protein of the blood plasma from 74.6 ± 1.24 to 62.4 ± 1.04 g/l (p<0.001) (Table 1), one of the reasons for which may be proteinuria.

| Groups of pregnant women | Control group | Metabolic syndrome |
|--------------------------|---------------|-------------------|
| Bx/ Indicators           |               |                   |
| Glucose, mmol            | 5.06 ± 0.1    | 5.82 ± 0.19<sup>11111111</sup> |
| HbA1c, %                 | 5.3 ± 0.18    | 5.61 ± 0.18       |
| Total protein, g / l     | 74.6 ± 1.24   | 62.4 ± 1.04<sup>11111111</sup> |
| Creatinine, μmol         | 88.14 ± 0.12  | 93.6 ± 0.14<sup>11111111</sup> |
| Total cholesterol, mmol / l | 5.04 ± 0.1 | 5.6 ± 0.19<sup>11111111</sup> |
| Malonic dialdehyde, mmol / ml | 2.93 ± 0.77 | 5.83 ± 0.16<sup>11111111</sup> |
| Catalase, mkat / l       | 213.55 ± 9.09 | 156 ± 12.4<sup>11111111</sup> |
| Superoxide dismutase, unitary act. | 68.33 ± 0.78 | 34 ± 0.11<sup>11111111</sup> |
| Ceruloplasmin, mg / l    | 257.25 ± 2.36 | 141 ± 3.06<sup>11111111</sup> |
| NO, μmol                | 53.19 ± 0.83  | 39 ± 1.27<sup>11111111</sup> |

Note: <sup>11111111</sup> - p<0.001; <sup>11111111</sup> - p<0.01; <sup>11111111</sup> - p<0.02; 1) p<0.05 reliability relative to control.

Table 1: Biochemical indicators of blood in pregnant women with metabolic disorders.

In the process of fetal development in pregnant women there is a violation of glucose utilization by tissues, which creates a certain deficit of energy-forming substrates. Incomplete aerobic oxidation of glucose, which does not result in the oxidation of reduced equivalents in the respiratory chain, promotes the formation and leakage from the electron transport chain of active metabolites of oxygen initiating the LPO process. The concentration of MDA is increased from 2.93 ± 0.77 to 5.83 ± 0.16 nmol/ml (p<0.01) (Table 1). On the other hand, activation of lipid peroxidation is facilitated by a decrease in the activity of AOS enzymes. The data showed that the accumulation of products of free radical oxidation lead to the depletion of the antioxidant system, a decrease in the activity of superoxide dismutase, catalase and ceruloplasmin concentrations (respectively, from 68.33 ± 0.78 to 34 ± 0.11 units (p<0.001); from 213.55 ± 9.09 to 156 ± 12.4 mcat/l (p<0.01), from 257.25 ± 2.36 to 141 ± 3.06 mg/l (p<0.001) (Table 1).

Thus, our studies in groups of pregnant women with metabolic disorders established the activation of LPO processes, according to the MDA increase of 98.97 compared with the control group (0.01), due to the formation of ROS and oppression of AOZ cells. Intensification of LPO in pregnant women with MS was observed against a background of a significant increase in the level of total cholesterol by 23.01 and 11.11% of LDL cholesterol, respectively, i.e. Atherogenic lipoproteins, relative to the control group (0.05).

Thus, the activation of lipid peroxidation in pregnant women with metabolic disorders (MS) is facilitated by the following factors: suppression of aerobic oxidation of glucose, resulting in a deficiency of reduced equivalents, a violation of the adequacy of the electron transport chain, dyslipidemia and tissue hypoxia [26,27]. In addition, under conditions of oxidative stress, the concentration of NO- the main vasodilating factor decreases from 53.19 ± 0.83 to 39 ± 1.27 μmol (p<0.01) (Table 1), which gives a vasoconstrictor effect. As a result, the latter is further aggravated by hypoxia, accompanied by narrowing of the vessels of microcirculation. A vicious circle is created that can
lead to profound functional and morphological disorders in the internal organs of the fetus and the pregnant woman [28,29].

Insulin resistance in pregnant women with MS can be more pronounced due to more intensive secretion of the contra-insulin hormones in the placenta in the mother and in the newborn, namely placental lactogen, chorionic gonadotropin, estrogens, progesterone, prolactin and cortisol [30-32].

One of the serious disturbances in energy metabolism with the enhancement of SRO is the separation of respiration and phosphorylation, and, consequently, the weakening of biosynthesis of macroergic compounds, especially ATP. This, in turn, inhibits the biosynthesis of proteins, nucleic acids and other compounds, which significantly affects the formation of the developing fetus. The results of the study are the basis for determining the parameters of LPO, AOS, carbohydrate and lipid metabolism and NO-forming endothelial function as additional laboratory tests for the purpose of timely assessment of metabolic disturbances in MS and prognosis for the pregnant and fetus [33].

**Conclusion**

Thus, in pregnant women with metabolic disorders, there is a violation of the adequacy of glucose oxidation and the functioning of the respiratory chain, activation of LPO, a decrease in the activity of AOS enzymes. AMC and LPO products lead to a decrease in the content of nitric oxide, the main vasodilating factor. Simultaneously, there is an increase in the content of OXc and LDL-C, Atherogenic LP. As a result of these changes, hypoxia develops, which significantly affects the formation of the developing fetus. Therefore, it is advisable to recommend the determination of indicators of the POL-AOS system, the exchange of cholesterol and the NO-forming endothelial function as additional laboratory tests in pregnant women with MS.

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