CLINICO-LABORATORY PARALLELS BETWEEN THE STATE OF LIPID SPECTRUM IN PREGNANT WOMEN WITH OVERWEIGHT AND PATHOLOGY OF THE FETOPLACENTAL SYSTEM: PRELIMINARY DATA

N.A. Negrusha

S.M. Kirov Military-medical academy, Saint-Petersburg, Russia

Nadezhda A. Nergusha
MD, gastroenterologist,
gastroenterology department
negrunya@mail.ru

Abstract

The article presents the data on the degree of influence of dyslipidemia on the state of fetoplacental complex. It was found that the excess production of low-density lipoproteins in mothers with nutrition-constitutional obesity is a risk factor for the formation of the fetus macrosomia. One of the possible causes of pathological dyslipidemia can be intra-hepatic cholestasis of the pregnant. The data obtained can be used in the practical work of the obstetrician-gynecologists, as well as therapeutists-practitioners in the field of extragenital pathologies of pregnant women.

Keywords

pregnant women, exogenous obesity, dyslipidemia, fetal macrosomia.

INTRODUCTION

The fundamental mechanism of physiological course of pregnancy consists in adequate restructuring of the endocrine system of the mother, which, in particular, is realized due to the formation of the placenta. The placenta secretes many different metabolic hormones – human chorionic gonadotropin, progesterone, estrogen, placental lactogen; the synthesis of glucocorticoids, thyroid hormones, with contrinsular and lipolytic action also increases. All this leads to the formation of transitive tolerance to glucose violations and dyslipidemia of a pregnant woman. In women with normal body mass these metabolism changes are physiological in nature and aimed at the adequate provision of a fetal with energy and plastic material. However, in case of mothers' overweight gestational restructuring of metabolism occurs on a background of already existing carbohydrate and lipid metabolism disorders, which, undoubtedly, leads not only to the aggravation of metabolism pathology in women, but also to various kinds of violations of fetoplacental complex.

RESEARCH OBJECTIVE

The purpose of this study was to explore some features of metabolism change in pregnant women with excessive body mass, as well as to evaluate their effect on the course of pregnancy and fetal development.

MATERIAL AND METHODS OF RESEARCH

The study included 45 pregnant at the later time period (the average gestational age 32,2±4,5 weeks), and 143 women in childbirth (the average term of pregnancy at the time of delivery was 39.8±1.3 weeks), who were in-patients of the clinic of obstetrics and gynecology of the Military-medical academy named after S.M. Kirov during from 2005 to 2010. The average age of the surveyed was 28.2±4.9 years. The main criterion for sampling was the presence of the mother's nutrition-constitutional obesity of different degree. The degree of obesity was assessed with the body mass index (growth, cm^2/weight, kg), calculated on the basis of the size and weight of the mother, specified in the prenatal record at the time of the registration in the antenatal clinic (the average term of pregnancy 11,2±2,4 weeks). The comparison group included 20 pregnant women and 19 practically healthy women of a representative of the age and the period of gestation.

All the pregnant women were analyzed from the point of their height, weight, concomitant therapy and

obstetric pathology diagnosed during this pregnancy, indicators of biochemical blood tests (total cholesterol, lipidogram, total protein, bilirubin, glucose, urea, ALT, AST). Additional parameters for the analysis in the group of mothers were complications developed in the period of confinement, and the anthropometric parameters of the newborn.

Statistical processing of the obtained data was performed on a personal computer using the package of applied programs "STATISTICA 8.0 for Windows".

STUDY RESULTS

The undertaken statistical analysis showed that the most significant changes in the groups of pregnant women and maternity cases concerned the laboratory indicators of biochemical blood tests, reflecting the state of metabolic processes. Thus, the estimate lipidogram revealed significant differences in the level of total cholesterol both in the group of pregnant (6.73±1.4 mmol/l vs 5.21±1.5 mmol/l in the control group), and in the group of mothers with overweight (8,48±1,4 vs 7,06±0.9 mmol/l in control group). A more detailed assessment of the level of cholesterol depending on the body weight of pregnant and women in childbirth, it was established that these differences concerned women with II degree of obesity and more. The degree of hypercholesterolemia correlates with the increase in weight of the newborn ($r=0.27$, $p<0.001$) and, respectively, with the increase of frequency of birth of children with body weight more than 4,000 grams ($r=0.45$, $p<0.05$).

The study of lipoprotein blood plasma subclasses showed that it was the level of low density lipoprotein that increased in the physiological course of pregnancy, compared with the established reference values for the Russian population outside pregnancy, while the concentration of lipoproteins of very low and high density almost did not change. However, in the case of the mother with II degree obesity, low-density lipoproteins significantly exceeded the average values obtained in the group of practically healthy women, $p<0.05$ (fig. 1). With the increase of the level of low density lipoprotein, as in the case of cholesterol, combined with the formation of macrosomia of the fetus and newborn ($r=0,25$, $p<0.05$ and $r=0,21$, $p<0.02$, respectively).

It is important to note here that the level of venous blood glucose, defined in pregnant women on an empty stomach, was not significantly different in the investigated groups from the relevant comparison group. Thus, the present data make it possible to formulate the assumption that the mass of the fetus is significantly affected not only by the level of glucose in the mother, but also by the content of low-density lipoprotein, which, in particular, through transition into free fatty acids, are actively used by the fetus as a source of energy and plastic material. At the same time, excess synthesis of low-density lipoproteins is a negative factor, which can lead to the formation of the fetus macrosomia.

Among the factors that exacerbated the dyslipidemia, besides the state of transient hyperinsulinemia on the background of tolerance to glucose violations, was developing intra-hepatic cholestasis of the pregnant. This was also confirmed in the course of this study: a positive correlation between the level of direct bilirubin, alkaline phosphatase and concentration in the blood plasma total cholesterol, as well as low density lipoproteins ($p<0.05$) was revealed. However, a significant difference between the groups which could enable to highlight the reference values of the liver functions, as one of the components of the stratification of the risk groups of the pregnant according to the possibility of pathological dyslipidemia wasn't revealed.

In addition to the fetus macrosomia, gestosis of different degree of intensity, spontaneous abortion, preterm birth, and intrauterine fetal hypoxia developed significantly more frequently in women with overweight compared with women with normal body weight. The incidence of preterm birth correlated with the level of low density lipoprotein ($r=0.24$, $p<0.05$). It is interesting to note that according to the statistical analysis, the frequency of the preeclampsia of the contrary was less than in groups with high cholesterol levels.

Thus, the existence of a women's nutrition-constitutional obesity of II degree and more is an extremely negative factor from the point of view of the forecast of the physiological course of pregnancy. At the same time, assessment of the distribution of the frequency of occurrence of obesity in young women has shown that it is at the age from 25 to 30 that women most frequently demonstrate the second degree of obesity, i.e. at the age reproductive activity of women.

DISCUSSION OF THE STUDY RESULTS

Dyslipidemia with a predominance of very low density lipoproteins, developing in women with normal body weight, is a physiological process. However, in case of the mother's nutrition-constitutional obesity of II degree and more the physiological process acquires a pathological character. It seems that in case of hyperproduction of low-density lipoproteins, even if the level of the mother's blood serum glucose remains within the normal limits, the fetus receives an excessive amount of energy and plastic material, which ultimately leads to the formation of the fetus macrosomia.

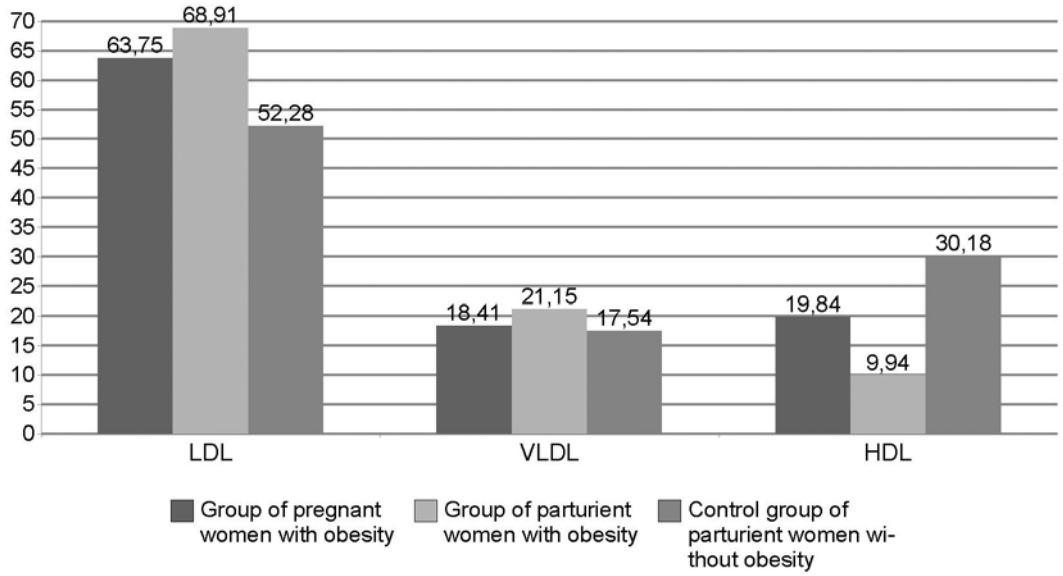

Figure 1. *The average of the level of low density (LDV), very low density lipoproteins (VLDL) and high density lipoprotein (HDL) in groups of pregnant and parturient women with exogenous obesity of the second degree.*

Probably permanent excessive content in the blood serum low-density lipoproteins is a factor in the development of spiral vessels of the uterus ateromatoza uterus, which creates conditions for the development of chronic fetal hypoxia, which increases the risk of premature birth. However, this theory requires further study.

There are many factors that lead to a change in blood serum lipid composition in pregnancy, but the main reason is still considered a hyperinsulinemia on the background of the gradual development of tolerance to glucose violations. At the same time one should not underestimate the contribution of functional changes of the hepatobiliary system in the form of intrahepatic cholestasis of pregnant women. As it is known that hyperestrogenemia, leading to disruption of the production of bile acids, is currently recognized as the alleged pathogenetic factor of development of gestational cholestasis. At the same time it is in the fatty tissue that aromatization of androgens to estrogens takes place. As a consequence of the fat tissue excess the production of estrogen, which aggravates holestasis, which in its turn contributes to the formation of pathological dyslipidemia, increases.

Thus, from the abovementioned, we can conclude that obesity is not only a present day problem, but a global problem of the future as well, as it is this disease that, in the view of its scale, makes a significant effect on the reproductive function of women and in the future may be a direct cause of the birth rate decline.

REFERENCES

1. **Blagosklonnaya Y.A.** Endocrinology: textbook for medical universities / Y.A. Blagosklonnaya, E.V.Shlyakhto, A.YU. Babenko. – 2 ed., corrected and augmented. – Spb.: SpetsLit, 2007. – 400 p.
2. **Golikova T.P.** Complications of pregnancy and childbirth in women with obesity [Electronic resource] / T.P. Golikova, Y.U. Durandin, N.A. Ermolova et al. //Bulletin of the Russian Association of the Obstetrician-gynecologists. – Electronic text is given. – 1999. – №2. – Mode of access: http://medi.ru
3. **Savelyeva G.M.** Obstetrics / G.M. Savelyeva, V.I.Kulakov, A.N. Strizhakov // – M: "Medicine", 2000. – 816 p.
4. **Citossi A.** Gestational diabetes: screening, management and follow up. 4th International symposium on diabetes and pregnancy: Program and abstract / Citossi A, Driul L. Peressini, L. et al. // Istanbul 2007: 29.
5. HAPO: Study Cooperative Research Group. Hyperglycemia and adverse pregnancy outcome // New Eng. G. Med. 2008; 358: 19: 1991–2002
6. World Health Organization: WHO Statistical Information Systems (WHOSIS) // World health statistics. – 2010. – P.175.