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THE IMPORTANCE OF DETERMINING HUMAN PLACENTAL LACTOGEN IN THE THIRD TRIMESTER OF PREGNANCY

ZNAČAJ ODREĐIVANJA HUMANOG PLACENTALNOG LAKTOGENA U TREĆEM TRIMESTRU TRUDNOĆE

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Summary: Human placental lactogen (HPL) is a hormone produced by the placenta with a role in the regulation of fetoplacental growth. In this paper, the results of HPL determination in the third trimester of pregnancy are presented with the aim of testing the sensitivity of this biochemical marker for detecting placental dysfunction, fetal vitality and risk of bad outcome. The tests were performed on 370 women with high-risk pregnancy, between the 20th and 36th week of pregnancy. HPL was determined by an ELISA method using *Bioserv Diagnostics* tests and the results were read by a *STAT-FAX 303+* reader. When compared to normal pregnancy, a significant decrease in the level of HPL biomarker was identified in preeclampsia ($p<0.01$), whereas in diabetes the serum level of HPL was significantly higher ($p<0.01$). A significant positive correlation between the level of HPL during pregnancy and the weight of a newborn child, its head circumference and Apgar score was obtained. The results of the research indicate that the maternal concentration of the HPL biomarker is directly connected to the vitality of placental tissue, so that HPL in the third trimester of pregnancy can be used as an indicator of placental insufficiency and fetal vitality.

Keywords: human placental lactogen, placental insufficiency

Kratak sadržaj: Humani placentalni laktogen (HPL) jeste hormon koji izlučuje placenta i regulator je fetoplacentalnog rasta. U radu su prikazani rezultati određivanja HPL-a u trećem trimestru trudnoće, sa ciljem da se ispita senzitivnost tog biohemijskog markera za otkrivanje poremećaja funkcije placente, vitaliteta fetusa i rizika za loš ishod. Ispitivanje je obavljeno na uzorku od 370 rizičnih trudnoća između 20 i 36 nedelje trudnoće. HPL je određen ELISA metodom, testovima »Bioserv Diagnostics«, a rezultati su očitani na rideru »STAT–FAX 303+«. Utvrđen je značajno snižen nivo biomarkera HPL kod preeklampsije u poređenju sa normalnom trudnoćom ($p<0,01$), dok je kod dijabetesa serumski nivo HPL značajno viši od normalnog ($p<0,01$). Ustanovljena je značajna pozitivna korelacija između nivoa HPL u trudnoći i težine novorođenčeta, obima glave i Apgar skora. Rezultati istraživanja ukazuju na to da je maternalna koncentracija biomarkera HPL direktno povezana sa vitalitetom placentalnog tkiva, te se HPL u trećem trimestru trudnoće može koristiti kao pokazatelj placentalne insuficijencije i vitaliteta fetusa.

Ključne reči: humani placentalni laktogen, placentalna insuficijencija

Introduction

Biochemical antenatal tests present biomarker analyses in maternal serum and urine, the concentration of which is dependant on fetal and placental physiology (1). The first hormone test in the observation of fetal vitality was the determination of estriol in maternal serum and urine, and later Human Placental Lactogen (HPL), which proved more sensitive in the observation of fetoplacental unit function, was discovered (2, 3).

Human placental lactogen (HPL) is a hormone produced by the placenta and has a role in the regulation of fetoplacental growth, so it is also known as the human chorionic somatotropin hormone (4). HPL is coded by the genes HPL-3 and HPL-4 within

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the HGH-V gene locus (human growth hormone variant gene) and stipulates the expression of normal placental function (5). Thyroid hormone (T3) stimulates the synthesis and release of the HPL hormone, one of the most important secretion products in the syncytiotrophoblast cells. It is determined in the serum of a pregnant woman, most often in the third trimester of pregnancy, and is used to indicate placental function (6).

Placental insufficiency leads to complications in pregnancy due to reduced nutritive placental function and oxygenation of the fetus leading to dysfunction of fetal growth and vitality. Certain conditions in a pregnant woman, such as hypertension, diabetes, kidney insufficiency, can lead to placental dysfunction. Normally, the concentration of the HPL hormone in maternal serum increases as the pregnancy progresses, whereas in the case of placental insufficiency its level decreases. A significant decrease of HPL has been identified in threatened abortions, bleeding, placental calcification, intrauterine fetal growth halt, intrauterine fetal death and in pregnancies which resulted in children born with fetal distress and asphyxia.

In the states of preeclampsia associated with hypertension, and the possible risk of toxemia, the determination of HPL biomarker can help us monitor placental function and fetal vitality after the 20th week of pregnancy. A significant increase in the secretion of HPL biomarker has been noticed in the states of hyperplasia of syncytiotrophoblast, diabetes, Rh incompatibility, placental trophoblast tumor and molar pregnancy. The aim of the research has been directed towards the study of HPL biomarker in the serum of women with high risk pregnancy and its connection with the pregnancy outcome.

Methods

The analysis of HPL biomarker was done in the Town Hospital in Subotica between 2002 and 2007. The tests were performed on 370 women with high risk pregnancy, between the 20th and 36th week of pregnancy. The indications for analyses were the states associated with a risk of preeclampsia, hypertension, kidney insufficiency, proteinuria and edema, diabetes, as well as ultrasonic detection of intrauterine fetal growth halt and a threatened abortion.

In high risk pregnancies, 46 with diabetes and 37 with preeclampsia, the HPL was checked three times in the third trimester of pregnancy. The HPL marker level in 50 normal pregnancies represented a control group.

HPL was determined by an ELISA method using *Bioserv Diagnostics* tests and the results were read by a *STAT-FAX 303+* reader.

The weight of a newborn child and the Apgar score were monitored in the first minute after the birth. Correlation between the level of HPL in the serum of a pregnant woman and the weight of a newborn child, its head size measurement and Apgar score was obtained. In the statistical calculation *t* – ratio was used (7).

Results

The HPL was determined in maternal serum three times in the third trimester of pregnancy, between the 24th and 36th week, and included two groups of women with high-risk pregnancy, 37 with toxemia and 46 with diabetes. Fifty normal pregnancies represented the control group (*Table I* and *II*).

Discussion

High-risk pregnancies are accompanied by two problems – the fetal weight, which is either small for the gestation age or too high, and prematurity. Both problems lead to high perinatal morbidity and mortality (8–9). A comparison of the HPL biomarker in high-risk pregnancy and normal pregnancy was made and it was noticed that the value of the biomarker in maternal serum in each tested week of the third trimester of pregnancy was significantly lower in preeclampsia and significantly higher in

Table I The values of HPL marker in the serum of a pregnant woman with high risk pregnancy and normal pregnancy.

HPL (mg/L) average value	Preeclampsia	Normal pregnancy	Diabetes
24–26 weeks	2.07 ± 1.75 t = 5.714	4.15 ± 2.55	6.22 ± 3.05 t = 7.341
28–30 weeks	3.36 ± 1.74 t = 1.985	5.6 ± 2.91	8.96 ± 4.46 t = 8.094
34–36 weeks	5.15 ± 1.47 t = 9.620	8.35 ± 3.35	11.19 ± 4.02 t = 1.460

24–26 weeks	p<0.01	df = 85 normal pregnancy – preeclampsia
	p<0.01	df = 94 normal pregnancy – diabetes
28–30 weeks	p=0.025	df = 85 normal pregnancy – preeclampsia
	p<0.01	df = 94 normal pregnancy – diabetes
34–36 weeks	p<0.01	df = 85 normal pregnancy – preeclampsia
	p=0.082	df = 94 normal pregnancy – diabetes

Table II The parameters of a newborn child in high-risk pregnancy and normal pregnancy.

Parameters (average value)	Preeclampsia	Normal pregnancy	Diabetes
Weight (g)	2895 *t* = 13.492	3314	4190 t = 16.197
Apgar/1 min	7.15 t = 15.348	9.2	8.56 t = 6.342
Head size measurement (cm)	32.9 t = 3.385	33.5	34.7 t = 8.710

Weight	p<0.01	*df* = 85 normal pregnancy – preeclampsia
	p<0.01	*df* = 94 normal pregnancy – diabetes
Apgar	p<0.01	*df* = 85 normal pregnancy – preeclampsia
	p<0.01	*df* = 94 normal pregnancy – diabetes
Head size measurement	p<0.01	*df* = 85 normal pregnancy – preeclampsia
	p<0.01	*df* = 94 normal pregnancy – diabetes

diabetes compared to normal pregnancy. There is a 99% probability ($p<0.01$) between the 24th and 34th week of pregnancy, which is very relevant, whereas probability is over 91% between the 34th and 36th week, meaning there is no significant loss of statistical quality. A high value of *t*–statistics indicates a considerable difference in the level of the HPL biomarker in high-risk pregnancy and normal pregnancy.

Similar results have been published by some other authors (10).

Maternal concentration of the HPL biomarker is directly connected to the vitality of placental tissue (11). Decreased concentration of the HPL marker in the serum in preeclampsia is conditioned by placental dysfunction.

The metabolism of carbohydrates and fat is also affected by human placental lactogen which can be responsible for diabetogenous status in high-risk pregnancies. (12, 13). Adipose tissues are also directly influenced by the activity of HPL hormone. Inadequate perfusion of placenta due to a higher resistance in uteroplacental circulation reduces the oxygenation of the intervillous space (14).

In hypoxia the mitotic activity of cytotrophoblast increases leading to its differentiation into syncytiotrophoblast. The production of human placental lactogen is increased in proliferous syncytiotrophoblast which has a diabetogenous effect, and thus explains the regular occurrence of gestational diabetes in high-risk pregnancies (15).

In this paper, a significant correlation between the level of HPL biomarker in the serum of a pregnant woman and the weight of a newborn child in normal pregnancies and pregnancies complicated by diabetes and preeclampsia ($p<0.01$) has been established. When HPL is low in the maternal serum of pregnant women suffering from preeclampsia, the weight at birth is significantly lower, whereas when HPL is higher in pregnant women suffering from diabetes, the weight of a newborn child is significantly higher in comparison to the weight of the babies born after normal pregnancies. This correlation between the level of HPL biomarker and the weight of a newborn child can be explained by its somatotrophic activity on a fetus. There is also a significant correlation between the level of HPL and the head size measurement of a newborn child in normal pregnancies and high-risk pregnancies affected by preeclampsia and diabetes ($p<0.01$). There is a significant correlation between HPL and the Apgar score in the first minute after birth ($p<0.01$) indicating that the HPL biomarker can be used as an indicator of fetal vitality.

The results of this study match with some other studies on the sensitivity of HPL biomarker published elsewhere in the world (16, 17). The results of the research have shown that HPL in the third trimester of pregnancy can be used as an indicator of placental insufficiency and disturbed fetal vitality. In high-risk pregnancies accompanied by preeclampsia and diabetes it should be controlled several times during pregnancy. Since placental dysfunction is related to disturbed oxygenation of the fetus, the determination of HPL biomarker in the third trimester of pregnancy has predictive characteristics. High-risk pregnancies must undergo regular clinical and laboratory control, glucose tolerance tests, ultrasonic control of fetal biometry and biophysical profile assessment, doppler tests of uteroplacental and fetoplacental circulation and, if necessary, monitoring of the labour itself.

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