Plasma lipids and lipoproteins in newborns of preeclamptic patients and normotensive pregnant women

Lípidos y lipoproteínas plasmáticas en neonatos de pacientes preeclámpticas y de embarazadas normotensas

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Resumen

Objetivo: Comparar las concentraciones de lípidos y lipoproteínas plasmáticas en neonatos de pacientes preeclámpticas con embarazadas normotensas.

Materiales y métodos: Se seleccionaron 100 pacientes que acudieron al Hospital Central "Dr. Urquinaona", Maracaibo, Venezuela. Los grupos consistieron en preeclámpticas (grupo A; n = 50) y embarazadas normotensas sanas (grupo B; n = 50), consideradas como controles. Se evaluaron las concentraciones de lípidos - lipoproteínas maternas y neonatales.

Resultados: No se encontraron diferencias estadísticamente significativas con relación a la edad materna y al índice de masa corporal materno entre ambos grupos (p = ns), pero si con respecto a la edad gestacional al momento del parto, presión arterial y proteinuria en 24 horas (p < 0,0001). Los neonatos del grupo A presentaron valores significativamente más bajos de colesterol y lipoproteínas de alta densidad comparados con los neonatos del grupo B (p < 0,0001). Las concentraciones de triglicéridos fueron más elevadas en los neonatos del grupo A comparado con aquellos del grupo B (p < 0,0001). Las concentraciones de lipoproteínas de baja densidad no mostraron diferencias significativas entre los dos grupos (p = 0,1224). No se observó correlaciones significativas entre las concentraciones de lípidos - lipoproteínas maternos y neonatales en el grupo A (p = ns).

Conclusión: Los recién nacidos de pacientes preeclámpticas tienen concentraciones significativamente más bajas de colesterol y lipoproteínas de alta densidad y concentraciones más altas de triglicéridos comparado con los recién nacidos de embarazadas normotensas sanas.

Palabras Clave: Lípidos, Lipoproteínas, Neonatos, Preeclampsia

Abstract

Objective: To compare plasma lipids and lipoprotein concentrations in newborn of preeclamptic patients with normotensive pregnant women.

Materials and method: A total of 100 patients were selected who assisted to Hospital Central "Dr. Urquinaona", Maracaibo, Venezuela. Groups consisted in preeclamptic patients (group A; n = 50) and healthy normotensive pregnant women (group B; n = 50) considered as controls. Maternal and neonatal lipids and lipoprotein concentrations were evaluated.

Results: There were not found significant differences related to maternal age and body mass index between groups (p = ns), significant differences were found in gestational age at time of delivery, blood pressure and 24-hour protein (p< 0.0001). Newborns of group A presented significant lower values of cholesterol and high-density lipoprotein compared to newborns of group B (p<0.0001). Triglyceride concentrations were higher in newborn of group A compared to those in group B (p <0.0001). Low-density lipoprotein concentrations did not show significant difference between groups (p = ns). There were not observed significant correlation between maternal and neonatal lipids - lipoprotein concentrations in group A (p = ns).

Conclusion: Newborns of preeclamptic patients have lower concentrations of cholesterol and high-density lipoprotein and higher concentrations of triglycerides compared to newborns of healthy normotensive pregnant women.

Keywords: Lipids, Lipoproteins, Newborn, Preeclampsia.

Introduction

In normal pregnancies without complications there are changes in the lipid profile. A gestational increment of 300% has been described in the concentrations of triglycerides (TG), 25-50% of total cholesterol and variations in the concentrations of high density lipoproteins (HDL-C) and low density lipoproteins (LDL-C)[1]. The physiological basis for this gestational alteration is the nutrient supply to the rapidly growing fetus and the maternal energy needs[2]. The placental transportation of cholesterol is possible through the uptake of LDL-C by a receiver on the maternal side. The maternal TG is hydrolyzed by lipoprotein lipase and transported through the placenta by the proteins that bind to fatty acids[3-5]. Hypertension syndrome during pregnancy is a specific multi-systemic disorder of pregnancy in humans and a maternal-fetal morbidity and mortality cause. The specific etiology is still unknown. It has been reported that in preeclamptic there is an alteration of the lipid profile, activation of leukocytes, increment of the inflammatory response and oxidative stress in the maternal circulation[6-8]. The hypoperfused placenta is the potential source of reactive oxygen species and cytokines that can induce maternal inflammatory response[9].

During preeclampsia, TG concentrations increase compared to what is observed in normal pregnancy, especially in the third trimester[1,10]. Concentrations of HDL-C reduce as a result of TG concentrations. The change of lipoprotein concentrations during preeclampsia is considered an adaptive response to the placental failure[1].

Few studies have focused on the circulatory changes such as biochemists in fetuses and newborn infants in preeclamptic women. Previous studies have shown that preeclampsia is associated with changes in the endothelial function of the fetal circulation[6]. However, there is little literature cited about the concentrations of lipids and lipoproteins in newborns of preeclamptic patients; therefore, the aim of this research was to compare the plasma concentrations of lipids and lipoproteins in preeclamptic patients with normotensive pregnant women.

Materials and methods

A study of cases and controls was carried out from January 2014 to June 2015, which included patients with simple pregnancies referred to the Hospital Central "Dr. Urquinaona", Maracaibo, Venezuela. A total of 100 pregnant women and their newborns were selected. Fifty preeclamptic and their newborns were included (group A) and a control group selected by having an age and body mass index similar to the study group, and consisted on 50 healthy pregnant women and their newborns (Group B). The research was approved by the Ethics Committee and Research of the hospital and a written consent of all patients was obtained.

Pregnant women with polyhydramnios, third trimester bleedings (placenta abruptio, placenta praevia), suspect of the intrauterine fetal growth restriction (head circumference, abdominal girth and femur length under 10 percent of reference with postnatal weight confirmation less than 10 percent of reference), HELLP syndrome, fetal heart rate abnormalities, multiple gestations, active maternal or intrauterine infection, chronic hypertensive disease (before 20 weeks of pregnancy), treatment with antihypertensive drugs, cardiac, liver or renal disease, pre or gestational diabetes mellitus, those pregnant women or newborns in which blood samples cannot be obtained and patients who have used drugs which alter plasma lipid concentration and smoking habit, were excluded. Also, patients who have refused to participate in the research were excluded. Preeclampsia was defined as systolic blood pressure of 140 mm Hg or more or diastolic blood pressure of 90 mm Hg or more, confirmed for 6 hours or more of difference, while the proteinuria is defined as 300 mg or more of protein in a 24-hour sample, or 1-2 proteinuria crosses in a qualitative examination after 20 weeks of gestation. Blood pressure was measured in the sitting position after 15 minutes of rest using a 14 cm-sleeve standard mercury upper-arm device. The systolic and diastolic blood pressure (taken in relation to the fifth Korotkoff sound) was compared to the 2 mm Hg nearest point. The palpatory method was used to verify the auscultation of systolic blood pressure readings. The systolic and diastolic blood pressures were calculated from the average of the blood pressure in each arm.

Blood samples (10 ml) were collected from the antecubital vein in all patients before giving birth and immediately after the diagnosis, and the sample was clotted at room temperature. Twenty milliliters of blood were placed in a tube with K2 acetic acid (1 mg/ml final concentration) and heparin. In the newly born the blood sample was obtained (5 ml) immediately after the birth. Plasma was stored at

-80°C, centrifuged at low speed and lipid and lipoprotein measures were done immediately after.

Plasma total cholesterol, TG and HDL-C measurements were performed by a modification of the standard protocol of research clinic of lipids, using enzymatic reagents for determining the lipids. Total cholesterol and TG were measured using automate enzymatic methods (COBAS® integrate cholesterol and COBAS® integrate triglycerides) on a Roche/Hitachi® 74 Analyzer. The concentrations of HDL-C were determined after the selective precipitation using manganese-heparin and after the enzymatic determination of cholesterol. The concentrations of LDL-C were calculated using the Friedwald formula (LDL-C = cholesterol - HDL-C - (TG/5)).

The data is presented as mean values ±standard deviation. The statistical analysis of the two groups was performed with the inference statistical test for unrelated data to compare the demographic characteristics and the lipid and lipoprotein concentrations. Pearson test was used to establish the correlations between maternal and newborn concentrations of lipids and lipoproteins. It was also used to establish the relationship between the lipid and lipoprotein concentrations and the weight of newborns. P<0.05 was considered statistically significant.

Results

The characteristics of preeclamptic women (group A) and normotensive pregnant women (group B) are shown in table 1. Statistically significant differences were not found in relation to the age and maternal body mass index (p = ns), but there were observed in the gestational age at the time of delivery, the systolic and diastolic blood pressure and 24-hour proteinuria (p<0.0001). It was observed that newborns of the patients from group A presented average weights significantly lower than newborn of pregnant women from group B (2872 ±309 grams compared to 3635 ±369 grams; p<0.0001).

Table 1. General characteristics

	GROUP A Cases (n = 50)	GROUP B Controls (n = 50)	p
Age/years	21.4 ± 3.0	22.1 ± 3.4	0.2777
Gestational age at the moment of the delivery, weeks	36.4 ± 1.1	38.3 ± 1.1	< 0.0001
Body mass index, Kg/m2	28.8 ± 2.0	28.9 ± 1.6	0.7831
Systolic blood pressure, mm de Hg	152.6 ± 18.2	119.2 ± 11.9	< 0.0001
Diastolic blood pressure, mm de Hg	96.6 ± 8.0	71.1 ± 9.0	< 0.0001
Proteinuria, g/24 horas	4.06 ± 1.87	0.12 ± 0.05	< 0.0001
Weight of the newborn, grams	2872 ± 309	3635 ± 369	< 0.0001

Table 2 shows the values of maternal and neonatal lipids and lipoproteins of the patients and infants in each group. The concentrations of cholesterol, TG, HDL-C and LDL-C were significantly more elevated in patients of group A compared to the patients of group B (p<0.0001). Newborns in group A had significantly lower values of cholesterol and HDL-C (74.9 ±10.4 mg/dL and 32.1 ± 3.6 mg/dL, respectively) compared to newborns of group B (89.3 ±10.7 mg/dL and 52.7 ± 2.8 mg/dL, respectively; p<0.0001). TG concentrations were higher in newborns of group A compared to those of group B (47.1 ± 8.0 mg/dL compared to 38.8 ± 6.4 mg/dL; p<0.0001). LDL-C concentrations did not show significant differences between the two groups (p = 0.1224).

Table 2. Maternal and neonatal lipid profile

	GROUP A Cases (n = 50)	GROUP B Controls (n = 50)	p
Maternal			
Cholesterol, mg/dL	311.0 ± 24.3	260.1 ± 26.9	< 0.0001
Triglycerides, mg/dL	342.1 ± 39.4	216.4 ± 29.1	< 0.0001
HDL-C, mg/dL	56.2 ± 3.8	50.2 ± 2.2	< 0.0001
LDL-C, mg/dL	181.8 ± 20.9	156.9 ± 24.0	< 0.0001
Newborn			
Cholesterol, mg/dL	74.9 ± 10.4	89.3 ± 10.7	< 0.0001
Triglycerides, mg/dL	47.1 ± 8.0	38.8 ± 6.4	< 0.0001
HDL-C, mg/dL	32.1 ± 3.6	52.7 ± 2.8	< 0.0001
LDL-C, mg/dL	39.3 ± 6.7	37.1 ± 7.4	0.1224

Significant correlations between the concentrations of cholesterol, TG and HDL-C were observed in all subjects of both groups (p<0.05) by correlating the concentrations of lipids and lipoproteins with maternal and fetal concentrations (table 3), but this correlation proved to be significant when they were analyzed in the group of cases and in the control groups, which may be due, in part, to the small number of cases in both groups (p = ns). The weight of newborn of preeclamptic women only showed weak, negative and significant correlation with concentrations of LDL-C neonatal (Figure 5; r = -0.299; p<0.05).

Table 3. Correlations in the parameters of the maternal/newborn lipid profile

	Both groups	Controls	Cases
Cholesterol	- 0.302*	0.143	0.199
Triglycerides	0.388*	0.067	- 0.221
HDL-C	- 0.664*	- 0.195	0.065
LDL-C	0.146	- 0.109	0.052

* p < 0.05.

Discussion

The results of this research confirm changes in the concentrations of lipids and lipoproteins in newborns of preeclamptic women compared to newborns of healthy normotensive pregnant women. On the other hand, the data from this current research

confirm previous findings of low concentrations of lipids in the newborns compared to maternal concentrations[4,5].

Normal pregnancy is associated with physiological hyperlipidemia, which is emphasized in preeclampsia[11]. In this research, preeclamptic women showed significantly higher values of TG compared to normal pregnant women. Different authors have reported that TG concentrations in preeclampsia may lead to an "atherogenic state" [12,13]. It has also been described that the increment of TG concentrations is a risk factor for cardiovascular disease[14].

Maternal TG does not cross the placental barrier, but the TG on maternal lipoproteins is hydrolyzed by lipase-placental lipoprotein and the resulting fatty acids are transferred across the placenta by proteins that bind to fatty acids. The positive regulation of this mechanism may increase the transport of fatty acids through the placenta to provide substrate to the fetal liver for the synthesis of TG[3,15]. Reaching the fetal circulation non- esterified fatty acids can be transported to the fetal liver for the synthesis of TG[3].

The findings of this research show the tendency to maternal hypertriglyceridemia and high concentrations of LDL-C in preeclamptic women compared to healthy controls, which has previously been reported[10,12,16]. Obesity is associated with dyslipidemia and abdominal-visceral fat correlates with increased plasma concentrations of TG and a decrease of HDL-C concentrations[17]. Body mass index is a risk factor for the development of preeclampsia and due to the influence of the body mass index on plasma lipids in pregnancy[18,19]. In this research, this possible confusing element was limited. It could be demonstrated by controlling the effects of the body mass rate on the lipid profile that the concentrations of lipids and lipoproteins in infants are affected by preeclampsia.

The metabolism of lipoproteins in the fetus is still unknown. In the fetus, the metabolism of HDL-C is different from the metabolism in adults[20]. The HDL-C forms a complex with the apoprotein E, the main acceptor of lipids and is captured by cells through the lipoprotein receptor. This movement of cholesterol plays an important role in the development of tissues. It is possible that maternal high concentrations of HDL-C may be involved in the transfer of cholesterol from the placenta to the fetal circulation by the ABCA1 transporter, which is highly expressed in this tissue[21]. HDL-C rich in apoprotein E is important in the redistribution of cholesterol from tissues, where they appear in high concentrations, to tissues that need cholesterol for the metabolic processes.

The increment of maternal lipids during preeclampsia may cause changes in the amount of lipids that cross the placenta, leading to modifications in the concentrations of neonatal lipids and lipoproteins. It is known that human placenta expresses large quantities of lipoproteins receptors and HDL-C receptors play an important role in the uptake of maternal lipoproteins for the steroid placental metabolism[22,23]. It has been shown that during the first trimester, trophoblast cells express SR-BI (a receiver of HDL-C) and it can work as effective supply route of cholesteryl esters of maternal lipoproteins to the fetal tissue[24]. It is important to mention that neonatal lipid profile did not provide significant correlations with values of maternal lipids and lipoproteins in preeclamptic women neither in normotensive pregnant women. This could indicate that the circulating concentrations of maternal lipids available for the placental uptake are not probably the main determinant of the lipid profile of infants.

Changes in lipids of newborns may be an appropriate physiological response to an adverse intrauterine environment. Transportation mechanisms can be modified to compensate the structural and oxidative damage of the placenta[25,26]. The concentration of lipids may alter due to an incomplete development or immaturity of biochemical processes involved in the metabolism. It has been reported that newborns who are small for their gestational age present alterations in the use of the circulating TG, consistent with the peripheral fat depletion[27]. Alterations in the lipid profile in infants of preeclamptic women can be attributed to the response of acute and chronic stress. Long-term stress can alter the fetal production of hormones such as cortisol, with effects on lipid metabolism.

The correlation observed between concentrations of LDL-C with the weight of the newborn of preeclamptic patients can be explained by the persistent decrease in the activity of the receptors of LDL-C associated with alterations in fetal liver growth[16,22]. Preeclampsia can lead to under-nourishment of the secondary fetus to utero-placental vascular insufficiency). The fetus responds to this state (particularly during the third trimester) keeping the brain growth at the expense of body growth[22]. This affects the liver, which grows rapidly in the last quarter, and it seems that it also affects the metabolism of LDL-C[16].

The data found in newborns of preeclamptic patients show high concentrations of cholesterol and TG with low concentrations of HDL-C. Therefore, the lipid profile of these infants would be, in relation to the group of control newborns, more atherogenic. These changes in the lipid profile of newborns of preeclamptic patients may have a negative effect during adulthood since it is related to the possible risk of atherosclerosis. Considering the changes in the lipid profile in this group of infants, it would be interesting to investigate if they have any difference in the risk factors compared to infants of normotensive pregnant women in a subsequent period. This can provide information about the metabolism of lipoproteins and, on the risk and importance of studying these subjects in the development of cardiovascular disease in adult life.

It is concluded that the infants of preeclamptic patients have significantly lower concentrations of cholesterol and

high-density lipoprotein, and higher concentrations of triglycerides compared to newborns of normotensive pregnant patients.

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