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Lipid profile in low birth weight newborns

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The aim of the study was to assess lipid metabolism in premature infants to identify common patterns depending on birth weight. The levels of cholesterol, triglycerides, high- and low-density lipoproteins were determined in 173 infants with moderately low birth weight, very low birth weight and extremely low birth weight, including infants with intrauterine growth restriction, each weight category recorded during the neonatal period. The study showed that extremely low birth weight newborns with intrauterine growth restriction and very low birth weight newborns had significantly lower levels of lipid profile than infants with moderately low birth weight. It is necessary to expand the study of methods for correcting lipid spectrum in low birth weight infants for rehabilitation of low birth weight infants.

Key words: CHOLESTEROL; FETAL GROWTH RETARDATION; LIPOPROTEINS; TRIGLYCERIDES

INTRODUCTION

Over the past fifteen years, the survival rate of low birth weight babies has increased significantly. However, further development of these children remains problematic. The vast majority of newborns with low birth weight have significant restrictions in growth and development during adaptation. About half of these newborns will lag in development in the future (1-3). Specific risk factors for impaired development and delayed pathology are not well understood (4, 5).

Currently, much attention is paid to the study of lipid metabolism during pregnancy and in newborns in the early neonatal period. Cholesterol and triglycerides are important components of lipid metabolism, providing necessary lipid metabolism and adequate development of the embryo and foetus. Cholesterol is crucial for foetal development throughout pregnancy, as it is an integral part of every cell membrane. The biosynthesis of foetal cholesterol, rather than transfer of cholesterol from maternal lipoproteins, is apparently the main mechanism for satisfying foetal needs in later stages of pregnancy (6, 7). The physiological and biochemical mechanisms of the passage of nutrients through the placenta are quite complex. According to studies, triglycerides do not pass from mother to foetus [8]. In earlier pregnancy, long chain polyunsaturated fatty acids can accumulate in the mother's body and can be transported across the placenta in later stages of pregnancy (9). Thus, a premature baby has a high risk of impaired lipid metabolism.

Transition from the intrauterine state to the extrauterine state is the most difficult adaptation that occurs in human life. Adaptation disorders are often detected after preterm delivery (10, 11). Moreover, the state of lipid metabolism is very important, as it provides the energy resource necessary for the adaptation of newborns and the protection of cell membranes from toxic metabolites.

Due to the low ability to break down and absorb lipids, premature babies can lose 10% to 40% of the fat obtained using a nutrient substrate (12, 13). Another 15% of fat is lost during oxidation and retention of adsorbed triglycerides in tissues, which reduces the use of triglycerides as an energy source. Therefore, a differentiated approach to replenishing energy resources in premature babies of varying degrees of maturity is of particular importance (14, 15).

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TABLE 1. Main characteristics of the low birth weight newborns studied

Variable	ELBW newborns		VLBW newborns		MLBW newborns	
	without IUGR (n=42)	with IUGR (n=17)	without IUGR (n=30)	with IUGR (n=38)	without IUGR (n=30)	with IUGR (n=16)
Gestational age (weeks)	25.8±1.5	29.2±2.2	29.4±1.1	33.6±1.2	32.4±1.5	36.6±0.8
Postconception age (weeks)	29.8±1.47	33.2±2.2	33.4±1.1	36.4±1.5	37.6±1.2	41.6±0.8
Formula feeding, n (%)	42 (100)	17 (100)	15 (50.0)	23 (61.0)	15 (50.0)	9 (44.0)
Extragenital pathology, n (%)	25 (59.5)	10 (58.8)	26 (86.6)	23 (60.5)	15 (50.0)	58 (50.0)
Preeclampsia/eclampsia, n (%)	32 (76.1)	11 (64.7)	18 (60)	28 (73.6)	2 (6.6)	1 (6.3)
Threatening miscarriage, n (%)	38 (90.4)	10 (58.8)	26 (86.6)	22 (57.9)	5 (16.6)	1 (6.3)
Uteroplacental insufficiency, n (%)	40 (95.2)	42 (100)	27 (90.0)	38 (100)	17 (56.6)	15 (93.7)
Placental abruption, n (%)	1 (2.3)	3 (17.6)	0	1 (2.6)	0	1 (6.3)
Smoking, n (%)	5 (11.9)	2 (17.6)	11 (36.3)	9 (23.6)	1 (3.3)	5 (31.2)

Continuous variables are presented as mean values with standard deviation, M±SD; binary variables presented as frequencies and percentages, n (%); ELBW = extremely low birth weight; VLBW = very low birth weight; MLBW = moderately low birth weight; IUGR = intrauterine growth restriction

The aim was prospective assessment of lipid metabolism in premature infants to identify common patterns depending on birth weight.

MATERIAL AND METHODS

Subjects

This study included 173 low birth weight (LBW) newborns with birth weight of 500-2,499 grams and gestational age of 23-37 weeks, including infants with intrauterine growth restriction (IUGR).

Study limitations: the study did not include infants with birth weight less than 500.0 grams; infants with birth weight more than 2499.0 grams; infants with gestational age less than 23 weeks; infants with gestational age over 37 weeks; infants with surgical pathologies; and infants with infectious diseases.

According to their birth weight, all newborns were divided into six groups:

1. 42 extremely low birth weight (ELBW) neonates (500 to 999 grams) without IUGR,
2. 17 ELBW neonates with IUGR,
3. 30 very low birth weight (VLBW) neonates (1,000 to 1,499 grams) without IUGR,
4. 38 VLBW neonates with IUGR,
5. 30 moderately low birth weight (MLBW) neonates (1,500 to 2,499 grams) without IUGR, and
6. 16 MLBW neonates with IUGR.

The main characteristics of newborns enrolled in this study are shown in Table 1.

Study protocol

LiquickCor-CHOL test systems (1974) were used to quantify cholesterol, triglycerides were measured using LiquickCor-TG test systems (1979), and high- and low-density lipoproteins were determined using the CORMAYHDLDIRECT test systems (1974). These parameters of lipid metabolism were measured on days 10 and 20 of life of the study newborns.

From the first day of life, ELBW and VLBW newborns were receiving parenteral nutrition in combination with minimal trophic nutrition (5-20 mL/kg). Enteral feeding of premature VLBW infants was initiated in the late neonatal period (12-18 days of life). The substrate of enteral nutrition was native breast milk or a specialized formula for premature and LBW babies. The group of MLBW newborns without significant disorders of neonatal adaptation were fed enterally from the first day of life (16). No breast milk additives were used.

The study was based on the analysis of the newborn serum content of the main indicators of lipid metabolism, such as cholesterol, triglycerides, high-density lipoproteins and low-density lipoproteins.

Statistical analysis

For continuous variables, descriptive statistics was reported as median (Me) and interquartile ranges (lower and upper quartiles, LQ, UQ) for non-normal distribution, and as mean (M) with standard deviation (SD) for normal distribution. We applied Shapiro-Wilk test to check whether the data were approximately normally distributed. Binary variables are presented as frequencies and percentages, n (%).

Mann-Whitney test was used to compare continuous variables among the groups. We used gamma correlation to

TABLE 2. Distribution of cholesterol, triglyceride, high-density lipoprotein and low-density lipoprotein levels according to weight category (mmol/L) and gestational age (day) of infants

Days	ELBW newborns		VLBW newborns		MLBW newborns	
	without IUGR (n=42)	with IUGR (n=17)	without IUGR (n=30)	with IUGR (n=38)	without IUGR (n=30)	with IUGR (n=16)
Chol on day 10	3.22 (3.02, 3.45)	3.08 (2.88, 3.24)	3.28 (3.05, 3.55)	3.13 (2.98, 3.34)	3.50 (3.30, 3.61)	3.16 (3.03, 3.27)
Chol on day 20	3.16 (3.02, 3.28)	3.12 (2.94, 3.21)	3.32 (3.06, 3.56)	3.22 (3.09, 3.42)	3.52 (3.23, 3.70)	3.21 (3.07, 3.43)
TG on day 10	0.88 (0.77, 0.98)	0.88 (0.74, 0.93)	0.94 (0.86, 1.02)	0.97 (0.93, 1.06)	0.95 (0.91, 1.05)	1.02 (0.94, 1.08)
TG on day 20	0.88 (0.85, 0.96)	0.78 (0.85, 0.88)	0.93 (0.88, 0.98)	0.94 (0.83, 0.98)	1.03 (0.96, 1.08)	0.99 (0.92, 1.04)
HDL on day 10	0.82 (0.76, 0.88)	0.86 (0.81, 0.92)	0.94 (0.84, 0.96)	0.88 (0.85, 0.95)	0.97 (0.94, 1.12)	0.97 (0.90, 1.10)
HDL on day 20	0.84 (0.82, 0.88)	0.85 (0.82, 0.92)	0.86 (0.81, 0.96)	0.92 (0.84, 0.98)	0.94 (0.88, 1.06)	0.97 (0.94, 1.06)
LDL on day 10	1.88 (1.76, 1.96)	1.84 (1.72, 1.88)	1.93 (1.84, 1.97)	1.84 (1.74, 1.96)	2.05 (1.87, 2.38)	1.92 (1.87, 2.14)
LDL on day 20	1.86 (1.78, 1.94)	1.88 (1.78, 1.94)	1.92 (1.86, 1.98)	1.92 (1.82, 1.96)	2.03 (1.87, 2.24)	1.98 (1.95, 2.18)
P_1:						
- Chol on day 10		0.065		0.089		**0.001**
- Chol on day 20		**0.041**		0.176		**0.009**
- TG on day 10		0.444		**0.038**		0.051
- TG on day 20		**0.006**		0.453		0.134
- HDL on day 10		0.383		0.428		0.706
- HDL on day 20		0.470		0.153		0.403
- LDL on day 10		0.202		**0.034**		0.247
- LDL on day 20		0.974		0.424		0.701
P_2:						
- Chol on day 10			0.276	0.190	**<0.001**	**0.198**
- Chol on day 20			0.066	**0.022**	**<0.001**	**0.032**
- TG on day 10			0.119	**<0.001**	**0.007**	**<0.001**
- TG on day 20			0.061	**0.001**	**<0.001**	**<0.001**
- HDL on day 10			**0.001**	0.111	**<0.001**	**0.002**
- HDL on day 20			0.229	0.112	**<0.001**	**0.005**
- LDL on day 10			0.234	0.498	**<0.001**	**0.006**
- LDL on day 20			**0.032**	0.265	**0.001**	**<0.001**
P Chol	0.565	0.605	0.807	0.455	0.673	0.513
P TG	0.434	0.209	0.895	**<0.001**	**0.024**	0.308
P HDL	**0.048**	0.820	**0.009**	0.495	0.075	0.313
P LDL	0.633	0.118	0.559	**0.033**	**0.006**	0.308

Data are presented as median with lower and upper quartiles, Me (LQ, UQ); P_1 = p-level of statistical differences (Mann-Whitney test) in newborns of similar weight (ELBW or VLBW or MLBW) without IUGR; P_2 = p-level of statistical differences (Mann-Whitney test) between ELBW newborns with and without IUGR; ELBW = extremely low birth weight; VLBW = very low birth weight; MLBW = moderately low birth weight; IUGR = intrauterine growth restriction; Chol = cholesterol; TG = triglycerides; HDL = high-density lipoproteins; LDL = low-density lipoproteins.

evaluate the strength of pair association between ordinal variable and continuous variable. To compare the variables within one patient group, we used Wilcoxon test. The point biserial correlation was used to measure the strength of pair association between the dichotomous variable and continuous variable.

RESULTS

The values of lipid content (cholesterol, triglycerides, high-density lipoproteins and low-density lipoproteins) obtained in the study newborns are shown in Table 2. We noted significant differences in their level among the groups of new-

borns (Table 2). The lowest cholesterol level was recorded in premature ELBW newborns with IUGR throughout the neonatal period (median 3.08 mmol/L). ELBW newborns without IUGR also had the lowest cholesterol among all infants in late neonatal age (median 3.16 mmol/L). However, in this group, there was a tendency to increase cholesterol levels in late neonatal age (median 3.12 mmol/L).

The lowest triglycerides levels were found in the groups of ELBW and ELBW with IUGR. They were the same in these groups in the early neonatal period (median 0.88 mmol/L). In the ELBW group with IUGR, the triglyceride level continued to decline in the late neonatal period (median 0.78 mmol/L).

The lowest high-density lipoproteins were observed in the groups of ELBW and ELBW with IUGR (median 0.82 mmol/L and 0.86 mmol/L, respectively), and in VLBW with IUGR in early neonatal age (median 0.88 mmol/L). In the latter group, high-density lipoprotein level increased in late neonatal age (median 0.92 mmol/L). The level of high-density lipoproteins did not change in the groups of ELBW and ELBW with IUGR in the late neonatal period (median 0.84 mmol/L and 0.85 mmol/L, respectively).

The same pattern was observed in the evaluation of low-density lipoproteins. The lowest low-density lipoprotein levels were observed in the groups of ELBW (median 1.88 mmol/L), ELBW with IUGR (median 1.84 mmol/L) and VLBW with IUGR (median 1.84 mmol/L) neonates. In the late neonatal period, low-density lipoprotein levels increased only in the ELBW group with IUGR (median 1.92 mmol/L).

DISCUSSION

This study showed that in ELBW newborns, the levels of the main indicators of the lipid spectrum, such as cholesterol, triglycerides, high-density lipoproteins and low-density lipoproteins, are significantly lower compared to LBW newborns. Although the analysis of lipid content in the examined newborns showed that their content was within the reference values, newborns with ELBW with IUGR had significantly lower levels of key lipid spectrum indicators, such as cholesterol, triglycerides, high-density lipoproteins and low-density lipoproteins, compared to newborns with LBW (17, 18). The significant differences can be explained by insufficient lipid intake, predominance of catabolic processes, deficiency of lipogenesis as a result of morphofunctional immaturity in extremely premature infants, and prenatal hypoxia caused by intrauterine pathology, as indicated in Table 1 (19, 20).

Similar results were obtained by *Maslovskaya* (17) and *Perepelitsa* (18). This can be explained by the fact that intensive lipid synthesis occurs at the end of a normal pregnancy, therefore, premature newborns lack the lipids in the early neonatal period due to high demands and low potential for their synthesis (4,21). However, these studies were conducted without taking into account trophic status at birth and in the early neonatal period, which is insufficient for complete analysis of lipid metabolism in all categories of premature infants in the neonatal period. A study by *Ramaraj et al.* (22), on the contrary, denies connection of lipid metabolism in foetuses and newborns with different body weights. However, the results of this study did not show differences in lipid levels in particular weight categories of premature babies and newborns with IUGR throughout the neonatal period. *Herrera* and *Ortega-Senovilla* (23) discuss the relationship of intrauterine pathology with lipid metabolism of newborns, not specifying its nature in different weight categories of these children. During late gestation, although maternal adipose tissue lipolytic activity becomes enhanced, lipolytic products cross the placenta with difficulty. Under fasting conditions, free fatty acids are used for ketogenesis by the mother, and ketone bodies are used as fuels and lipogenic substrates by the foetus. Maternal glycerol is preferentially used for glucose synthesis, saving other gluconeogenic substrates such as amino acids for foetal growth. Placental transfer of triglycerides is null, but essential fatty acids derived from maternal diet, which are transported as triglycerides in lipoproteins, become available to the foetus owing to the presence of both lipoprotein receptors and lipase activities in the placenta. However, premature infants do not have time to enter this metabolic period, as they are born before it begins. Therefore, changes in the maternal lipid profile are not significantly associated with average concentrations of total cholesterol, low- and high-density lipoproteins and triglycerides in premature newborns (24).

Accordingly, it is necessary to expand the study of methods for correcting lipid spectrum in LBW infants for their efficient rehabilitation.

CONCLUSION

The results of the study pointed to the importance of birth weight in assessing lipid metabolism in premature infants. The lowest level of all components of the lipid spectrum (cholesterol, low- and high-density lipoproteins and triglycerides) is due to the extreme immaturity of newborns in combination with IUGR. Cholesterol and triglyceride levels in newborns with ELBW and IUGR tend to decrease throughout the neonatal period, while high-density and low-density lipoprotein levels increase in the late neonatal period. The data obtained may be significant for further research aiming to determine effective methods of enteral and parenteral nutrition of premature infants.

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SAŽETAK

Lipidni profil u novorođenčadi niske porođajne mase

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Cilj istraživanja bio je procijeniti metabolizam lipida u nedonoščadi kako bi se utvrdili češći uzorci ovisno o porođajnoj masi. Razine kolesterola, triglicerida, lipoproteina niske i visoke gustoće mjerene su u 173 novorođenčadi umjereno niske, vrlo niske i iznimno niske porođajne mase, uključujući novorođenčad s intrauterinim zastojem rasta, a svaka se težinska kategorija bilježila tijekom neonatalnog razdoblja. Istraživanje je pokazalo da novorođenčad iznimno niske porođajne mase s intrauterinim zastojem rasta i novorođenčad vrlo niske porođajne mase ima značajno niže razine lipidnog profila nego novorođenčad umjereno niske porođajne mase. Potrebno je proširiti istraživanje metoda za ispravljanje lipidnog spektra kod novorođenčadi niske porođajne mase radi njihove rehabilitacije.

Ključne riječi: KOLESTEROL; INTRAUTERINI ZASTOJ RASTA; LIPOPROTEINI; TRIGLICERIDI