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Gestational diabetes mellitus has no affect on prohepcidin and other iron status parameters in infants

Cukrzyca ciążowa nie wpływa na stężenie prohepcydyny i wybranych parametrów gospodarki żelazem u noworodków

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ABSTRACT

Background: Hepcidin is a major iron regulatory protein. The aim of this pilot study was to determine hepcidin precursor –prohepcidin and iron metabolism parameters in serum cord blood of infants delivered by gestational diabetes mellitus mothers (GDM).

Materials and methods: The study group comprised 12 infants delivered by women diagnosed with GDM. The control group consisted of 18 full-term healthy infants. In the serum cord blood were measured: prohepcidin, ferritin and soluble transferrin receptor (sTfR).

Results: There are no significant differences in prohepcidin, ferritin and sTfR concentration in serum cord blood between infants delivered by GDM mothers and healthy infants.

Conclusion: Gestational diabetes mellitus has no affect on prohepcidin and other iron status parameters in infants.

Key words: Iron, Prohepcidin, Gestational diabetes mellitus, Newborns

STRESZCZENIE

Wstęp: Hepcydyna jest głównym białkiem regulującym gospodarkę żelazem. Celem tego pilotażowego badania była ocena stężenia prekursora hepcydyny – prohepcydyny i wybranych parametrów gospodarki żelazem w surowicy krwi pępowinowej noworodków urodzonych przez matki z rozpoznaną cukrzycą ciążową (GDM).

Materiały i metody: Grupę badaną stanowiło 12 noworodków urodzonych przez matki z rozpoznaną cukrzycą ciążową. Grupę kontrolną stanowiło 18 zdrowych noworodków urodzonych o czasie. W surowicy krwi pępowinowej oznaczono stężenie prohepcydyny, ferrytyny i rozpuszczalnego receptora transferyny (sTfR).

Wyniki: Nie stwierdzono istotnie statystycznych różnic w stężeniu prohepcydyny, ferrytyny i sTfR pomiędzy grupą badaną a grupą kontrolną.

Wniosek: Cukrzyca ciążowa nie wpływa na stężenie prohepcydyny i innych parametrów gospodarki żelazem noworodków.

Słowa kluczowe: żelazo, prohepcydyna, cukrzyca ciążowa, noworodki

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Introduction

Gestational diabetes mellitus (GDM) is a general complication during pregnancy, which affects 2–9% pregnant woman [1]. According to Buchanan et al. GDM is a glucose intolerance of various degrees that is first detected during pregnancy [2]. It has been shown that

Table 1. The characteristic of women chosen to study **Tabela 1. Charakterystyka kobiet włączonych do badania**

Parameter Parametr	GDM mothers Mean (range) Matki z cukrzycą ciążową Średnia (zakres)	Healthy mothers Mean (range) Zdrowe matki Średnia (zakres)
Number Liczebność	12	18
Age (years) Wiek (lata)	29 (20–35)	30 (20–38)
Number of pregnancies Liczba ciąż	(1–3)	(1–3)
Parity Liczba porodów	(1–3)	(1–3)
Model of delivery Rodzaj porodu	Vaginal delivery Poród główkowy, siłami natury	Vaginal delivery Poród główkowy, siłami natury

Table 2. The characteristic of study and control group **Tabela 2. Charakterystyka grupy badanej i grupy kontrolnej**

Parameter Parametr	Study group Mean (range) Grupa badana Średnia (zakres)	Control group Mean (range) Grupa kontrolna Średnia (zakres)
Number Liczebność	12	18
Gestational age (weeks) Wiek ciążowy (tygodnie)	40 (36–42)	40 (38–42)
Birth weight (g) Masa urodzeniowa (g)	3499 (2970–4370)	3495 (2710–4480)
Birth length (cm) Długość urodzeniowa (cm)	55 (51 – 62)	55 (50–62)
APGAR score at 1st min APGAR w pierwszej minucie	9 (5–10)	9 (9–10)
Gender (F/M) Płeć (D/C)	3/9	11/7

F: female, M: man D: dziewczynki, C: chłopcy

GDM is associated with various perinatal complications. GDM is related to lower gestational age at delivery, fetal macrosomia, hyperinsulinism and obesity development in childhood and early adulthood [3–6]. What is more, mothers diagnosed with GDM have higher risk of developing type 2 diabetes mellitus [7].

Hepcidin (l*iver-expressed antimicrobial protein*, LEAP-1), a small protein synthesized mainly in hepatocytes, is a essential regulator of iron homeostasis. This protein bounds to ferroportin (*solute carrier family 40* (*iron-regulated transporter*), *member 1*, SLC40A1), the sole cellular iron exporter, causing its internalization and degradation, what decreased serum iron concentration [8]. It has been shown in few experimental and clinical studies that ferroportin is expressed in placental syncytiotrophoblast, but precisely role of hepcidin and ferroportin in iron transport from maternal to fetus circulation has not been completely identified yet [9-10]. Previous clinical researches have also shown link between iron metabolism and GDM, even in cases of non-iron deficiency anemia GDM women [11–14]. To our knowledge this is the first paper that has describing prohepcidin concentration in serum cord blood of infants delivered by GDM mothers. The aim of this study was to determine prohepcidin, ferritin and sTfR in serum cord blood of infants delivered by GDM mothers compared with matched non-diabetic full-term healthy controls.

Methods

The study group comprised 12 infants (gestational age 36–42 weeks) delivered by women diagnosed with GDM. The control group consisted of 18 full-term healthy infants (gestational age 38–42 weeks). The characteristic of mothers is listed in Table 1.

Table 3. Prohepcidin, ferritin and sTfR levels in serum cord blood of study and control group

Tabela 3. Stężenie prohepcydyny, ferrytyny i sTfR w surowicy krwi pępowinowej w grupie badanej i grupie kontrolnej

Parameter Parametr	Study group Grupa badana			Control group Grupa kontrolna			p
	n	Me	Q1;Q3	n	Me	Q1;Q3	
Prohepcidin [ng/ml] Prohepcydyna [ng/ml]	12	75.00	61.45; 103.06	18	69.19	47.69; 79.68	NS
Ferritin [ng/ml] Ferrytyna [ng/ml]	12	67.90	22.46; 88.01	18	57.21	34.42; 72.44	NS
sTfR [µg/ml] sTfR [µg/ml]	12	3.84	2.31; 6.24	18	3.13	2.60; 4.43	NS

Me: median, n: number, NS: non-significant, p: probability value, Q1: lower quartile, Q3: upper quartile, sTfR: soluble transferrin receptor.

Me: mediana, n: liczebność, NS: różnica nieistotna statystycznie, p: p-wartość, Q1: kwartyl dolny, Q3: kwartyl górny, sTfR: rozpuszczalny receptor transferyny.

All women were tested at the beginning of the third trimester with a 75g oral glucose tolerance test (OGTT) administered in the morning after an overnight fast. The diagnosis of GDM was based on adequate glucose concentration in serum: fasting ≥4,8 mmol/l, 1h ≥10,0 mmol/l, and 2h ≥8,7 mmol/l. The characteristic of the study and control groups is present in Table 2. This study was approved by the Ethics Committee of Ludwik Rydygier Collegium Medicum in Bydgoszcz (Poland).

After uncomplicated vaginal delivery blood samples from the umbilical vein were obtained before placenta expulsion and clumping of the umbilical cord. The blood samples were then centrifuged (2000 x g for 20 min., tem. +4°C) and serum were stored at -80°C until examination.

In the serum cord blood were measured: prohepcidin (ELISA test, DGR Instruments GmbH, Marburg, Germany), ferritin (ELISA test, DRG International Inc., USA) and soluble transferrin receptor (Human sTfR ELISA, BioVendor Laboratory Medicine Inc., Czech Republic).

Statistical analysis was carried out using the STATISTICA® 9.1 for Windows (StatSoft, Cracow, Poland). The Mann-Whitney U-test was used for statistical analyses. Data are expressed as a median (Me) and lower (Q1) and upper (Q3) quartiles. Correlation coefficients were determined by Spearman's test and p less than 0,05 was considered a statistically significant.

Results

The results of iron metabolism parameters are summarized in Table 3. There are no statistically significantly differences in prohepcidin, ferritin and sTfR concentration in serum cord blood between infants delivered by GDM mothers (n=12) and healthy infants (n=18). We haven't observed any significant correlation between prohepcidin, ferritin and sTfR in both groups (p>0,05).

Discussion

The relationship between GDM and iron was previously reported but it is the first report that has describing concentration of hepcidin precursor – prohepcidin and other iron metabolism parameters in serum cord blood of infants delivered by GDM mothers [11-14].

Ervasti et al. described that serum prohepcidin in healthy pregnant women was significantly higher in comparison to the serum cord blood prohepcidin in full-term newborns [15]. There was also significant correlation between the maternal and newborn serum prohepcidin concentration, however level of prohepcidin did not correlate with ferritin and sTfR concentration [15]. The same situation was observed by Chełchowska et al. [16]. They reported that serum prohepcidin in healthy, pregnant women and in cord blood of their newborn has not correlated with ferritin, transferrin and total iron levels [16]. Furthermore, serum cord blood prohepcidin was statistically significant lower in comparison to the prohepcidin concentration in mothers [16]. Study by Tiker et al. demonstrated no significant correlations between levels of serum prohepcidin, ferritin, iron and transferrin in 16 healthy term and 26 healthy preterm newborns [17]. Congruent prohepcidin concentration in serum cord blood of appropriate for gestational age newborns was described by Amarilyo et al. [18]. The mean prohepcidin level was

similar to observed in our control group [18]. What is more, they have shown no significant difference in serum cord blood prohepcidin levels between newborns small for gestational age and newborns appropriate for gestational age [18]. Results from this paper were similar to those reported by Balogh et al. [19]. In 20 healthy neonates mean serum cord blood prohepcidin was alike to our results, but mean ferritin level was almost two fold higher than observed in our control group [19]. Note, however, that ferritin concentration in Balogh and colleagues work was very wide (range 56–328 ng/ml) [19].

In conclusion, our preliminary results suggest that gestational diabetes mellitus has no affect on prohepcidin and other iron status parameters in infants. Future studies should describe also hepcidin levels in serum cord blood of infants delivered by women diagnosed with GDM. The relationship between glucose intolerance in mothers and iron status in fetuses needs to be examined.

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