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Lipid metabolism characteristics in women of child-bearing age with iron-deficiency anemia

Ralnikova N.A.[2*], Kalev O.F.[1]

[1]South Ural State Medical University, Chelyabinsk, Russia
[2]Chelyabinsk Regional Hospital №1, Chelyabinsk, Russia

Authors:

Nadezhda A. Ralnikova, M.D., Ph.D., the head of the therapy department №1, Chelyabinsk Regional Hospital №1, Chelyabinsk, Russia

Oleg F. Kalev, M.D., Ph.D., doctor of sciences, professor of the department of hospital therapy, South Ural State Medical University, Chelyabinsk, Russia

Summary

Objective

To determine interrelation between lipid metabolism characteristics with iron-deficiency anemia and other cardiovascular risk factors in women of child-bearing age.

Materials and methods

Using the results of complex population study of rural dwellers, we performed analysis of lipid metabolism characteristics and other cardiovascular risk factors in 506 women of child-bearing age.

Results

Women with iron-deficiency anemia (n=26) had significantly lower levels of total cholesterol (p=0,009), low density lipoproteins cholesterol (p=0,003) and significantly lower atherogenic index (p=0,003). Regression analysis demonstrated that the presence of iron-deficiency anemia is an independent factor that significantly reduces the possibility to have atherogenic dyslipidemia in females of studied population (OR=0,20, 95% CI 0,07-0,55, p=0,002).

Conclusion

It is recommended to take into account the presence of iron-deficiency anemia in case of investigation of lipid metabolism characteristics in women of child-bearing age.

Key words

iron-deficiency anemia, hemoglobin, dyslipidemia, cholesterol.

* Corresponding author. Tel. +7-906-893-23-35. E-mail: ralnikovana@mail.ru

Introduction

In 1981 J.L.Sullivan proposed that levels of serum iron in women of child-bearing age lower comparing with men have protective action against atherogenesis [1]. Several studies in models of donors with atherosclerosis and hemochromatosis have been conducted, and their results are controversial [2-7]. Iron-deficiency anemia (IDA) could have become another model for testing J.L.Sullivan's hypothesis. The study of relation between IDA and known cardiovascular risk factors, first of all, such surrogate atherosclerosis signs like lipid metabolism characteristics appears to be possible in this case [8]. There are single evidences related to lipid metabolism characteristics and based on clinical observation in patients with IDA. The features of lipid metabolism characteristics in females of child-bearing age with IDA in relation to known cardiovascular risk factors are not studied enough in population level.

The objective of this study was to determine interrelation between lipid metabolism characteristics with IDA and other cardiovascular risk factors in women of child-bearing age

Materials and methods

This work has been performed as a part of the Countrywide Integrated Noncommunicable Diseases Intervention (CINDI) program. We conducted a complex epidemiological study of the dwellers of Muslumovo village (Chelyabinsk region) on the base of Chelyabinsk Regional Hospital №1 diagnostic center involving wide spectrum of professionals (physician, gynecologist, surgeon, neurologist, ophthalmologist, etc). Population involvement reached 93%. All patients signed informed consent. Patients underwent physical examination, laboratory tests (complete blood count, urine test, urea, creatinine, bilirubin, glucose, lipids' blood levels), spirometry, electrocardiography (ECG), abdominal and kidney echography, and additional laboratory and instrumental tests, if it was necessary.1242 females aged 18-82 years have been observed. Exclusion criteria were: acute posthemorrhagic anemia, anemia of chronic disease, megaloblastic anemia, cancer, thyroid gland disorders (hypothyroidism, hyperthyroidism), diabetes mellitus, severe hepatic disorders with clinical and laboratory signs of active process (hepatic depression, syndromes of cytolysis and cholestasis), any malabsorption syndrome, chronic alcoholism and drug addiction, active phase of kidney disorders and/or nephrotic syndrome, chronic kidney failure, acute myocardial infarction, infectious diseases (acute and exacerbations of chronic disorders), systemic connective tissue disorders, pregnancy. We excluded patients with non-iron deficiency anemia and patients with possible secondary disorders of lipid metabolism.

We selected medical records of 506 women according with inclusion/exclusion criteria. IDA diagnosis was established according with the WHO guidelines, if hemoglobin (Hb) blood levels were <120 g/L or if there was erythrocyte hypochromia (color index) and reduced concentration of serum iron (<12 mmol/L). IDA was detected in 26 female patients (average age 35.7±7.5 years), the control group included 480 women without IDA (average age 33.4±7.9 years). There were no significant differences of age between women with IDA and the control group (p=0.80). The majority of IDA cases were related to uterine bleeding (18 cases), less frequently they were caused by nasal (4 cases) and hemorrhoidal bleeding (4 cases).

Morphological composition of peripheral blood was investigated using standard laboratory techniques. Hb levels were evaluated using Sahli's hemoglobinometer, number of erythrocytes and leukocytes was estimated using cell-counting chamber, platelets were quantified using Fonio's method. Leukocyte count was performed using samples stained with Romanowsky method and visualized using light microscopy. Total cholesterol (TC), triglycerides (TG), high density lipids cholesterol (HDL Ch) levels were determined using reagents of "Human" company (Germany) and "Hitachi" machine (Japan). Serum concentration of iron was evaluated using reagents of "Human" company (Germany) and "Flexor E" (Netherlands) machine.

We developed a specific questionnaire that allowed us to estimate cardiovascular risk factors. Cardiovascular risk factors were estimated using WHO criteria (1995). Low physical activity (LPA) was described as staying in sitting position for more than 5 hours per day in case of less than 10 hours of physical activity per week or intensive physical activity less for less than 30-40 minutes per day. Character of alcohol consumption within the last year was estimated using J Merta's classification [10]. Burdened family history included sudden death, acute myocardial infarction, stroke, early development of arterial hypertension (AH) (before the age of 65 years in women and before 55 years in men) in the relatives of the first degree of kinship. AH was diagnosed if blood pressure (BP) levels were ≥ 140/90 mm Hg after two measurements. Body mass index (BMI) was quantified

using the following formula: BMI=body weight / (body height^2, m^2). BMI between 18 and 24.9 kg/m^2 was considered normal, excessive body weight started from BMI⩾25 kg/m^2.

Impairment of lipid metabolism and dyslipidemia type were diagnosed according with the guidelines of dyslipidemia diagnosis and management [8]: TC ⩾ 5.0 mmol/L, TG ⩾ 1.7 mmol/L, HDL Ch < 1.2 mmol/L, LDL Ch ⩾ 3 mmol/L. LDL Ch concentration was quantified using W.T. Friedewald's formula [11]: LDL Ch (mmol/L) = TC = HDL Ch – 0.45*TG. Atherogenic index (AI) was estimated using A.N. Klimov's formula [12]: AI = TC/HDL Ch. The presence of IIa, IIIb, III, and IV dyslipidemia types was considered as atherogenic impairment of lipid metabolism.

Results were analyzed using STATISTICA 6.0 software [13]. We chose statistical test after performing normality test. Results are present as M±σ, where M is average value, σ – root-mean square deviation in case of normal distribution, and as Me (25; 75), where Me is median, 25 and 75- 25th and 75th percentiles, respectively if the distribution was different from normal. If the distribution was normal, comparison of quantitative characteristics was performed using Student's τ-test, if the distribution was not normal, Mann-Whitney test was used. The odds ratio (OR) was quantified with 95% confidence interval (CI) using EpiInfo 5.16 software. To evaluate relation between the characteristics of lipid metabolism and risk factors we made multiple logistic regression analysis. P-value <0.05 was considered significant.

Results

Women with IDA had significantly lower TC, LDL CH, and AI levels comparing with the women of the control group (p=0,009, p=0,003, p=0,003, respectively) (Table 1).

There were no statistically significant differences in the structure of atherogenous dyslipidemias (AD) between two groups (x^2=0.75, p=0.73). Dyslipidemia, IIa type prevailed in both groups (Table 2).

The frequency of lipid metabolism abnormalities in the group of women with IDA and in the control group was 15.4% and 41.9% for dyslipidemia, IIa type and 19.2% and 47.9% for other AD, respectively. The chance to have IIa type dyslipidemia and other AD in women with IDA was significantly lower comparing with the women of the control group (OR=0,25, 95% CI – 0.07-0.79, p=0.07 for dyslipidemia IIa type and OR=0.26, 95% CI 0.08-0.74, p=0.04 for other AD types) (Table 3, 4).

Regression model of AD demonstrated that age, BMI and burdened family history were independent factors that significantly increased the probability of AD in women of child-bearing age. The presence of IDA was an independent factor that reduced significantly the chance to have AD in the studied population (Table 5).

Table 1. **Lipid metabolism characteristics in women with IDA and control group women, Me (25, 75)**

Characteristics	IDA, n=26		Control, n=480		p
	Me	(25; 75)	Me	(25; 75)	
TC, mmol/L	4.23	3.46-4.80	4.87	3.90-5.60	0.009*
TG, mmol/L	0.88	0.68-0.99	0.93	0.64-1.11	0.9
LDL CH, mmol/L	2.55	1.93-2.92	3.18	2.38-3.82	0.003*
HDL CH, mmol/L	1.28	1.14-1.48	1.27	1.10-1.47	0.8
AI	3.33	2.89-3.79	3.96	3.11-4.50	0.003*

Comment: * - p< 0,05.

Table 2. **The frequency of lipid metabolism disorders in women with IDA and women of the control group, absolute number and %**

Dyslipidemia type	IDA, n=26		Control, n=480	
	abs.number	%	abs. number.	%
IIa type	4	15.4	201	41.9
IIb type	0	0	18	3.7
III type	1	3.8	4	0.8
IV type	0	0	7	1.5
Total number o AD cases	5	19.2	230	47.9

Comment: abs.number – absolute number

Table 3. **The frequency of cardiovascular risk factors in women with IDA and in control group women, abs. number, %**

Risk factor	IDA, n=26		Control, n=480	
	abs.number	%	abs. number.	%
Burdened family history	10	38.5	174	36.3
AH	18	69.2	365	76.0
Increased body weight	14	53.9	294	61.3
AH	5	19.2	84	17.5
Excessive body weight	15	57.7	262	54.6

Comment: abs.number – absolute number

Table 4. **OR for cardiovascular risk factors in women with IDA and women of the control group**

Risk factor	OR	95% CI for OR	p
Burdened family history	1.10	0.45-2.63	0.82
AH	0.71	0.28-1.83	0.43
Increased body weight	0.74	0.31-1.74	0.45
AH	1.12	0.36-3.26	0.79
Excessive body weight	1.13	0.48-2.71	0.76

Table 5. **AD multiple regression analysis model (logistic regression)**

Risk factor	OR	95% CI for OR	p
Initial value	0.02	0.01-0.07	<0.0001*
Age	**1.07**	**1.04-1.11**	**<0.0001***
IDA	**0.22**	**0.08-0.60**	**0.004***
LPA	0.84	0.57-1.25	0.39
Alcohol consumption	0.80	0.51-1.25	0.32
Burdened family history	**1.52**	**1.03-2.24**	**0.034***
AH	0.73	0.43-1.25	0.25
BMI	**1.06**	**1.02-1.11**	**0.008***
Total significance of the model			<0.0001*

Comment: * - p< 0,05.

Discussion

For the first time we demonstrated that women of child-bearing age with IDA have significantly lower levels of the main atherogenic lipid fractions comparing with the control group women of the same age. We discovered for the first time that IDA could be an independent factor that reduced significantly the probability to develop AD. Our results support the hypothesis of J.L. Sullivan.

Single clinical studies demonstrated antiatherogenic shift in blood lipid spectrum in case of IDA [14-15]. The study of Zhelobov and coauthors demonstrated positive correlation between the number of erythrocytes and concentration of proatherogenic lipids in IDA and revealed the correlation between changed lipid spectrum and severity of anemia.

It has been demonstrated that the role of iron in atherogenesis is related to lipid peroxidation and inflammation [16-18]. Xanthine oxidase, mieloperoxidase, lipoxygenase have iron atoms, by this iron participates in enzymatic part of lipid peroxidation. OH-groups can be produced through non-enzymatic reaction between peroxides and metalloproteinases. Hydrogen peroxide's decomposition in Fenton's reaction in the presence of Fe^{2+} leads to formation of hydroxyl radical. Iron up-regulates tumor necrosis factor- α (TNF- α) expression. Pre-latent and latent iron deficiency decreases the activity of macrophages. From one side, it leads to impaired immune system activity associated with IDA, from another side, it can have a protective effect on atherogenesis.

We think that it is impossible to explain lower values of atherogenic lipid fractions and lower frequency of dyslipidemia just by the effect of iron. It is necessary to consider other factors like hemic hypoxia that leads to compensatory hemodynamic effects and requires further investigation. The mechanism of hipolipidemic effect in IDA is related to the action of enzymatic systems of erythrocytes' cytoplasm [19], hypoxia action [20], and possible reduction of liver synthetic function. Authors consider this phenomenon as a compensatory-adaptive reaction on hypoxia that leads to increased resistance of erythrocyte' membrane. Thus, reduction of cholesterol levels in IDA can be related to its mobilization for erythrocytes' survival in anemia. Antiatherogenic shifts in lipid spectrum can be present in blood malignancies.

Our results are very relevant for further theoretical and practical studies. It is recommended to take into account the presence of IDA while investigating lipid metabolism characteristics in women of child-birth age.

Conclusion

Women with IDA had significantly levels of TC, LDL Ch, and AI levels comparing with the women from the control group

The possibility to have IIa type of dyslipidemia and any AD in women with IDA was significantly lower comparing with the control group.

Important characteristics of lipid metabolism in women with IDA do not depend on the other cardiovascular risk factors.

Conflict of interest: None declared.

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