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RESEARCH ARTICLE

Structure and function of erythrocyte membranes in moderate degree iron-deficiency anemia in early-age children in mountain conditions

Asankul A. Kucherbaev[1], Jury V. Borjakin[2], Kubat S. Ibraimov[3], Aigul B. Cherikchieva[1]

[1]Department Hematology, National Centre for Protection of Motherhood and Childhood, Bishkek, Republic Kyrgyzstan, [2]Chair of Hospital Pediatrics Course Neonatology Kyrgyz State Medical Academy, Bishkek, Republic Kyrgyzstan, [3]Department Nuclear Magnetic Resonance Imaging, National Centre for Protection of Motherhood and Childhood, Bishkek, Republic Kyrgyzstan

Correspondence to: Asankul A. Kucherbaev, E-mail: caerc.usue@gmail.com

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ABSTRACT

Background: The paper presents data on the structure and the function of erythrocyte membranes in moderate degree iron-deficiency anemia (IDA) in early-age children living in mountain conditions. **Aim and Objectives:** Explore pathogenic mechanisms for membrane destructive disorders in IDA in the early-age children living in the high-mountain area and develop a program for diagnostics and reasonable kinds of etiopathogenetic therapy. **Materials and Methods:** Research was made in high-mountain regions of the Kyrgyz Republic. A clinical supervision was made in dynamics with a focus on a structure of peripheral blood, maintained phospholipids fractions detected in erythrocytes membranes with a method of thin-layer chromatography on Silufol plates and with a quantitative definition of phosphorus by Barlet’s method. **Result:** In IDA in children in the mountain area, there is a disorder in phospholipids between blood plasma and red blood cells with an accumulation of the lizoform. **Conclusion:** The paper presents the findings that relate to pathogenic mechanisms for disorders in the phospholipid composition of erythrocytes membranes in moderate degree IDA among 170 early-age children living in the high mountains zone in the Kyrgyz Republic. The paper also includes the indicators and presents results saying of a positive dynamic in specific membrane phospholipids of erythrocyte disorders liquidation in the treatment with a preparation of iron sulfate with folic acid.

KEY WORDS: Early-age Children; Erythrocytes; Iron-deficiency Anemia; High Mountains

INTRODUCTION

The World Health Organization (WHO) has estimated that globally 1.62 billion people are anemic with the high prevalence (47.4%) of anemia among preschool children.[1,2] A condition of erythrocytes membranes in moderate degree iron-deficiency anemia (IDA) in early-age children (first 3 years of the life) was a stage in previous research. It is worth mentioning that a course of IDA in mountain conditions has pathogenic-morphologic features in comparison with conditions of low-mountain and flat regions. These features relate to an influence of combined hemic hypoxia and natural hypoxic hypoxia of high-mountain area on a child’s body. Such a complex influence on children of the first years of the life has a high importance in a course of anemia, for the treatment efficiency and in many respects; it finally defines a disease outcome.[3,4]

Therefore, an increase at the beginning of functional, and then structural changes to organs and tissues, a decrease in

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arterial and tissular oxygen is a basis for a similar hypoxia-associated inability of the oxygen transport system of the body to fulfill its own function in full.[5-7]

Research Purpose

The research in pathogenic mechanisms of membrane-destructive disorders, how they occur with IDA in the early-age children in conditions of high mountains and development of a program of diagnostics and rational variants for the etiopathogenetic therapy.

MATERIALS AND METHODS

The research was done in high mountainous areas of the Republic of Kyrgyzstan, i.e., in Naryn (2.020 m above sea level) and Suusamyr (2.280 m above sea level). 170 early-age children with moderate degree IDA (according to the WHO classification, the erythrocyte number is 2.5×10^{12}/l-3.0×10^{12}/l, an indicator of hemoglobin is 70.0-90.0 g/l) were under supervision. 40 healthy children were surveyed as a control group.

To diagnosticate a disease and monitor the results from the received treatment, the following methods were used: A clinical supervision in dynamics, an analysis of a structure in peripheral blood,[8] a definition for maintenance of phospholipids fractions in erythrocytes membranes with a method of thin-layer chromatography on Silufol plates and a quantitative definition of phosphorus according to the method of Barlet.[9] The research was made in compliance with the declaration of Helsinki.

RESULTS

As the research has shown, in the phospholipid structure of erythrocyte membranes in the surveyed patients, in comparison with the control group, expressed changes are observed (Table 1). Along with an increase in maintenance of total phospholipids (TP) ($P < 0.01$), fractions of lysophosphatidylcholine (LPC), phosphatidylserine (PS), phosphatidylethanolamine (PEA) ($P < 0.05$) raise and the maintenance of fractions sphingomyelin (SPM) ($P < 0.01$), phosphatidylcholine (PC) ($P < 0.01$) decreases that lead to an increase in a value of the coefficient saying of a relation between easily oxidizable (PS, PEA) to difficult oxidizable (SPM, PC).

These changes show that in the mountain conditions in IDA children have a disorder in phospholipids between the blood plasma and erythrocytes with an accumulation of lysoforms, in particular, LPC due to a blockade of metabolic ways of a transformation of this metabolite into PC and a disorder in processes of LPC inhibition and its elimination from a body. The processes that in a complex influence an increase in the maintenance of LPC in erythrocyte membranes are certainly adverse for a structurally functional organization of a membrane and a cell as a whole due to inhibition of catalytic centers of fibers-enzymes of a bio membrane with a subsequent disorder in permeability, transport, fluidity and stability of membranes, a change to the erythrocyte form.

Table 1: Indicators of phospholipid structure of erythrocyte membranes in early-age children with moderate degree IDA in conditions of high mountain areas

Analyzed indicators of phospholipid structure	Statistics indicators	Analyzed groups	
		Healthy children (*n*=32)	Children with IDA (*n*=62)
TP (mcg) P_n	M±m *P*	33.43±3.632	48.082±2.248 <0.01
LPC (%)	M±m *P*	6.7±0.401	7.5±0.201 <0.05
SPM (%)	M±m *P*	22.6±0.824	20.3±0.024 <0.05
PC (%)	M±m *P*	25.5±1.147	22.6±0.086 <0.05
PS (%)	M±m *P*	21.7±1.146	24.3±0.067 <0.05
PEA (%)	M±m *P*	23.0±1.29	25.9±0.002 <0.05
$\frac{PS \pm PEA}{SPM \pm PC}$	M±m *P*	0.961±0.054	1.203±0.038 <0.01

TP: Total phospholipids, LPC: Lysophosphatidylcholine, SPM: Sphingomyelin, PC: Phosphatidylcholine, PS: Phosphatidylserine, PEA: Phosphatidylethanolamine, IDA: Iron-deficiency anemia

A reduction in PC in membrane complexes in the surveyed patients confirms its resynthesize reduction that leads to a decrease in the PC antioxidatic role and PC in the cellular structure.

A reduction in the SPM maintenance in erythrocyte membranes leads to a decrease in protective properties of erythrocytes, the acidotic shifts in blood plasma, a change to electrostatic properties in red blood cells and an increase in permeability of a membrane.

The increasing FS fraction content and PEA and the coefficient (FS±PEA)/(SFM±PC) shows an increase in the proportion of polyunsaturated fatty acids in easily oxidizable fractions of phospholipids, which leads to disruption of the structural organization of lipid phase in cell membranes, processes of an active transport through the cell membrane and an enzyme activity of biological membranes.

Because of the provided treatment with the iron preparation (iron sulfate with folic acid), there were expressed changes

Table 2: Indicators of phospholipid structure for erythrocytes membranes in early-age children with moderate degree IDA in conditions of high mountains in time of treatment termination

Analyzed groups	Statistical indication	TP (mcg) P_n	Phospholipids fractions (%)					PS ± PEA / SPM ± PC
			LPC	SPM	PC	PS	PEA	
Healthy children (*n*=32)	M±m	33.43±3.632	6.7±0.401	22.6±0.824	22.6±1.147	21.7±1.146	23.0±1.29	0.961±0.054
Children with IDA before treatment (*n*=62)	M±m	48.8±5.248	7.5±0.201	20.3±0.421	22.6±0.386	24.3±0.467	24.9±0.502	1.203±0.038
Children with IDA in time of treatment termination (*n*=26)	M±m	29.53±4.0	8.9±1.242	21.9±0.906	25.0±1.007	20.2±0.896	26.9±1.136	1.01±0.064
	P_{3-1}	<0.05	<0.05	>0.05	>0.05	>0.05	<0.05	>0.05
	P_{3-2}	<0.01	>0.05	>0.05	<0.05	<0.05	>0.05	<0.05

TP: Total phospholipids, LPC: Lysophosphatidylcholine, SPM: Sphingomyelin, PC: Phosphatidylcholine, PS: Phosphatidylserine, PEA: Phosphatidylethanolamine, IDA: Iron-deficiency anemia

to described processes. Hence, in the phospholipid structure of erythrocyte membranes (Table 2) in comparison with time before treatment, we observe an authentic decrease in maintenance of TP ($P < 0.01$), an increase in PC fraction ($P < 0.05$) and a decrease in PS, a value of coefficient PS+PEA/SPM+PC is ($P < 0.05$). In comparison with the control indicators, the maintenance of fractions LPC and PEA has remained as increased ($P < 0.05$).

DISCUSSION

It is necessary to consider the described changes to phospholipid structure of erythrocyte membranes in the surveyed patients in terms of mechanisms of the lipid turnover in erythrocyte membrane, where the basis for the acylation reaction include specific enzyme acetyltransferase, magnesium, and adenosine triphosphate (ATP). First, these changes occur in fractions of the most metabolic-active phospholipids, namely, PC and PEA. Deviations from a standard for the membrane structure of erythrocytes occur because of a disorder in these reactions accompanied by a change to the osmotic resistance and hemolytic processes.

Disorders in LPC acylation with free fat acid for PC formation lie at the heart of these changes. Fat acid can also join PEA, as well as PC, but in this case, it serves as a substratum endogenic lysophosphatidylethanolamine. PC and PEA can liberate fat acids, as a return of free fat acid back to plasma is a catabolic process. Besides, there is a specific mechanism to transport fat acid with PC and PEA; this mechanism is a basis for almost 1/3 fat acids exchange. As a result, there is a series of phospholipase and transmutase reactions to remove LPC surplus. In the surveyed patients, this series of reactions decreases, owing to what LPC collects in erythrocyte membranes.

It is also connected with a decreasing, along with these active reactions, passive transport of inclusion of fat acid for their lipid structure preservation. Because of the reduced inclusion of fat acid into PC in erythrocytes, its concentration decreases. On the contrary, inclusion in PEA is raised, and its concentration raises. A general consequence of this metabolic disorder is a disorder of phospholipid structure of erythrocyte membranes. In turn, it can cause a disorder in a function of a membrane, in particular, its permeability for basic cations (sodium, potassium, magnesium, and calcium). Along with it, the disorder in a metabolism of fat acid can be caused by the nonspecific early inhibition to include fat acid in erythrocyte phosphatides. Such inhibition can be caused by a decrease of erythrocytes ATP stocks at the expense of the glucose deficiency *in vitro*.

CONCLUSIONS

The findings have shown that combined hemic and hypoxic hypoxia in the early-age children leads to an intensification in POL processes and a general reorganization of the erythrocytes phospholipid structure with its fatty acid structure change, and hence, to a disorder in the phase condition. The usage of iron sulfate with folic acid to treat moderate degree IDA does not only result in an increase in hemoglobin concentration in erythrocytes but also leads to the restored erythrocyte membranes structure. These findings are from the fact that hemoglobin is bio antioxidant in a human body and that there is a change to its concentration, and naturally structurally influence functional properties of bio membranes.

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