INFLUENCE OF MOUNTAIN-CLIMATIC THERAPY ON THE LEVEL OF SERUM LIPIDS AND LIPOPROTEINS IN PATIENTS WITH APLASTIC ANEMIA

K.A. Aitbaev[1], B.K. Aisarieva[2], O.A. Igemberdieva[1], L.B. Rezepkina[1], A.R. Raimjanov .[2]

[1] Research Institute of Molecular Biology and Medicine at the National Centre of Cardiology and Internal medicine named after Academician M. Mirrakhimov;

[2] Kyrgyz Scientific Center for Hematology, Bishkek, Kyrgyz Republic.

Abstract

The influence of mountain-climatic therapy on serum lipids and lipoproteins level was determined in 29 patients with aplastic anemia. It is shown, that mountain-climatic therapy promotes serum lipids and lipoproteins levels normalization, increasing their content at hypolipidemia and, in contrast, reducing their content at hyperlipidemia. The positive changes tend to persist 6 months after patients' discharge from high-altitude hospital.

Key words: lipids, lipoproteins, mountain-climatic therapy.

INTRODUCTION

Aplastic anemia (AA) relates to severe blood diseases with high morbidity and mortality rates in patients. In the absence of timely and adequate treatment, 80% of cases with AA die within three months from the start of manifestation the disease.

In recent decades, there has been significant progress in the treatment for aplastic anemia with application of specific therapy methods, such as bone marrow transplantation and immunosuppressive therapy. However, the above-mentioned treatment methods may not always be available to most patients due to their high cost. In addition, the specific methods are fraught with side reactions, which sometimes complicate directly the disease problems. These circumstances today compelling the scientists to search for alternative treatment ways for AA that may be more available on the one hand and have a high therapeutic efficacy with minimal side effects on the other one.

Kyrgyz researchers have achieved major advances in substantiation and development of the so-called method of a mountain-climatic therapy (MCT) that applies practically over the period of half a century. This method positively influence the clinical course of diseases with depression of hemopoiesis, contributing to a significant reduction in manifestations of anemia and hemorrhagic syndromes, an alleviation of the disease, a prolongation of the remission and stabilization of hematological parameters (1,2,3).

Studies of the mechanisms of positive influence of mountain climate on the clinical course of disease with depression of hemopoiesis, performed by Kyrgyz scientists were marked by the

obtaining of new clinical evidences and test data, including data at the molecular level, however, a question of mountain climate influence on the patients' body with AA is in need of further analysis, studying and refinements (4). From this position, a research oriented to study the alterations of serum lipids and lipoproteins content in patients with AA under the influence of the natural conditions of hypoxia, is of particular interest. Given that, firstly, lipids are of vital importance to cell activity and, secondly, abnormalities in their metabolism, in particular, hypolipidemia and hyperlipidemia may cause alterations of blood corpuscle functionality, the performing of the previously mentioned study may reveal new mechanisms of the positive influence of mountain climate on the clinical course of AA.

Purpose of this study is to investigate the dynamics of serum lipids and lipoproteins level in patients with AA during and 6 months after the end of MCT.

MATERIALS AND METHODS

29 patients with AA (18-58 years) were examined during the course of their 40-day adaptation to the high altitude hospital (Tuya-Ashuu pass, 3200 m above sea level). Samples of blood for lipids testing was taken from the cubital vein after overnight fast of 12 hours in the morning before climbing a mountain height, on the 5th, 10th, 20th and 40th days of high-altitude adaptation. After that, the blood was centrifuged, and then a separated serum was aspirated and stored in sealed vials in a refrigerator at -20 ° C for one month (no more than). On the testing day, the serum was heated to 20 ° C, and then mixed well and the lipid testing was carrying out.

Cholesterol (C) and triglycerides (TG) concentrations were tested with a hematology analyzer "Hospitex" using a Rendox reagents kit. Levels of high density lipoprotein cholesterol (HDL-C) were determined by the method of A.N. Klimov and I.E.Ganelina (5). The method principle is that apoB-containing low-density lipoproteins (LDL) and very-low-density lipoproteins (VLDL) are flocculated by the action of heparin in the presence of manganese ions, at the same time HDL remain in the supernatant. It is there a content of HDL cholesterol is determined.

LDL-C was determined by the following formula: LDL -C = total cholesterol (TC) - (TG / 2.2+ HDL -C). The ratio of TG / 2.2 corresponds to the content of VLDL-C (6,7).

Data statistical analysis was carried out with the definition of means and error of mean value ($X \pm m$) in the groups under comparison. Accuracy of the mean values difference was determined using Student's t-test. Differences were considered reliable if the coincidence probability of means was less than 5% ($p < 0.05$).

RESULTS AND DISCUSSION

It was found that the average rates of total cholesterol (TC), triglycerides, HDL-C, LDL-C and VLDL-C did not change significantly at the general group of patients after staying in the high-altitude hospital (Table 1).

Data on the dependence of lipid corrective effect of adaptation to hypoxia from the initial level of lipids (8,9,10) were obtained previously. Therefore, we divided the examined patients into 3 groups basing on the initial level of total cholesterol: group I (n = 11) included patients with hypocholesterolemia (initial level of total cholesterol <3.88 mmol / L), group II (n = 12) included patients with normocholesterolemia (initial level of total cholesterol = 3.88 - 4.99 mmol / L) and group III (n = 6) - patients with hypercholesterolemia (initial level of total cholesterol = 5.0 mmol / L or more). Analysis of total cholesterol concentration in each of these groups has shown that the initial level of total cholesterol is important in determination of the direction of its concentration shift under the influence of staying in the high-altitude hospital.

Table 2 data show that the concentration of total cholesterol level has significantly increased in group of patients with initially low level of TC (<3.88 mmol / L) already on the 10-day of MCT (3,44 ± 0,08 and 3,84 ± 0,12 mmol / L in patients before and at day ten of MCT, respectively; P <0,05). In contrast, the concentration of cholesterol level in the group of patients with initially high levels of TC, has reduced and to day 40 of adaptation achieves significant values (5,73 ± 0,26 and 4,56 ± 0,28 mmol / L in patients before and at day 40 of adaptation, respectively; P <0,05). In group II (normo-holesterolemia) significant changes in the concentration of total cholesterol did not happen (4,36 ± 0,07 and 4,42 ± 0,17 mmol / L in patients before and at day 40 of adaptation, respectively; P >0.05).

Other test indices (triglycerides, HDL cholesterol, LDL cholesterol and VLDL cholesterol) show similar tendency in the shift direction (decrease - at initially high levels and increase - at initially low). However, the significance of these changes was accurate only for LDL cholesterol in patients with hypercholesterolemia (3,15 ± 0,14 and 2,50 ± 0,22 mmol / L in patients before and at day ten of adaptation; P <0,05) .

Thus, adaptation to high altitude had a two-way influence on blood lipids in patients with AA: it increased their level at the initial hypolipidemia and decreased at initial hyperlipidemia. That is, differential vector in both the first and the second case was directed towards normalization of lipid metabolism indices. Finally, and it is very significant, that the therapeutic effect of a mountain climate therapy of patients with AA tends to persist over 6 months after the MCT completion (Table 2).

This fact can be considered as one of the hypothetically possible molecular mechanisms that base therapeutic effect of mountain-climatic therapy in patients with AA. Red blood cells do not synthesize cholesterol and its content in them depends on the exchange with plasma lipoproteins cholesterol. Therefore hypocholesterolemia causes a significant reduction of cholesterol content in red-cell membranes, changing the ratio of cholesterol and phospholipids in them. As a result red-cell membrane permeability increases, cavities and cribriform structures form on its surface,

through which the direct hemoglobin molecular flow leak occurs. In contrast, hypercholesterolemia causes cholesterol accumulation in the red-cell membrane, as a result membranes permeability is reduced and its microviscosity increased (11).

Thus, in both the first and the second case substantial changes occur in the lipids content of plasma membrane, that damage membrane structure and affect its function. If plasma membrane is considered to be of vital importance to cell activity, including their biological functions (12), positive changes identified during MCT in serum lipids concentrations in patients with AA, directed to their normalization, and therefore to lipids content of red-cell membranes normalization, can be considered as one of the possible molecular mechanisms of the positive influence of high altitude adaptation on the disease clinical event.

CONCLUSION

Thus, the study results brings us to the conclusion that mountain-climatic therapy promotes serum lipids and lipoproteins level normalization, increasing their content at hypolipidemia and, in contrast, reducing their content at hyperlipidemia. The changes are positive, as they are directed to the red-cell membrane normalization that increases their functional activity. Consequently, changes in serum lipids and lipoproteins content identified by us in patients with AA can be considered as one of the possible molecular mechanisms of the positive influence of high altitude adaptation on the disease clinical event.

REFERENCES:

1. Mirrakhimov M.M., Raimjanov A.R. Dynamics of changes of red blood cells during the high-mountain climatic adaptation and the experience of mountain-climatic treatment for patients with certain blood diseases. In: Molecular aspects of adaptation to hypoxia. Kiev: Naukova Dumka 1979:181-204.

2. Raimjanov A.R. Clinical presentation and hematopoiesis in patients with cytopenic syndromes and iron deficiency anemia at high altitude (Dissertation), Frunze-Moscow, 1988, 434 p.

3. Raimjanov A.R. Aplastic Anemia and Mountain Climate. Bishkek, 2002: 304.

4. Raimjanov A.R., Tsopova I.A., Astapova S.G., Eralieva M.O. High-altitude climate for the treatment of patients with depression of hematopoiesis. Central Asian Medical Journal 2012; 1:100-104.

5. Klimov A.N., Ganelina I.E. Phenotyping of dyslipoproteinemia (Guidelines). Moskow,1984:16.

6. Rifkind B. Typing of hyperlipoproteinemia. Atherosclerosis 1970; 11:545-546.

7. Friedewald W.T., Levy R.I., Fredrickson D.S. Estimation of the concentration of low-density lipoprotein cholesterol in plasma without use of the preparative ultracentrifuge. Clin. Chem.1972; 18:499-502.

8. Aitbaev K.A. Influence of altitude adaptation and nutrition on parameters of lipids metabolism and the prevalence of coronary heart disease in the Kyrgyz SSR (Dissertation), Moscow, 1990, 260 pp.

9. Aitbaev K.A., Kim N.M., Brimkulov N.N. Influence of short-term high altitude adaptation on human serum lipoproteins. Aviakosm. Ekolog. Med. 1992; 5-6:93-95.

10. Mirrakhimov M.M., Aitbaev K.A., Murataliev T.M., Kim N.M. Possibility of correcting atherogenic dyslipoproteinemia by the mountain climate treatment. Cardiologiia 1991; 31:8-10.

11. Kroes J., Ostwald R., Keith A. Erytrocyte membranes – compression of lipid phases by increased cholesterol content. Biochim. Biophys. Acta 1972; 274:71-74.

12. Maxfield F.R., Tabas I. Role of cholesterol and lipid organization in disease. Nature 2005; 1:43(7068):612-621.

Table 1

Dynamics of serum lipids and lipoproteins level in general group of patients with aplastic anemia during and 6 months after mountain-climatic therapy completion (X ± m)

Parameters	n	Initial rate	Mountain-climatic therapy (days)				After 6 months
			Day 5	Day 10	Day 20	Day 40	
TC (mmol/L)	29	4.3±0.15	4.3±0.13	4.3±0.15	4.3±0.13	4.3±0.11	4.4±0.11
TG (mmol/L)	29	1.6±0.15	1.6±0.13	1.5±0.13	1.6±0.11	1.6±0.11	1.7±0.13
HDL-C (mmol/L)	29	1.3±0.07	1.3±0.07	1.3±0.07	1.4±0.06	1.4±0.06	1.3±0.06
LDL-C (mmol/L)	29	2.3±0.11	2.3±0.13	2.3±0.09	2.2±0.07	2.2±0.07	2.3±0.11
VLDL-C (mmol/L)	29	0.7±0.07	0.7±0.06	0.7±0.06	0.7±0.06	0.7±0.06	0.8±0.05

Note: Differences between the initial data and the data obtained in the subsequent examination periods are not significant for all investigated parameters (P> 0.05)

Table 2

Dynamics of serum lipids and lipoproteins level in patients with aplastic anemia combined with initial hypo-, normo-, and hypercholesterolemia during and 6 months after mountain-climatic therapy completion (X ± m).

Patient groups (gr)	Initial rate	Mountain-climatic therapy (days)				After 6 months
		Day 5	Day 10	Day 20	Day 40	
TC (mmol/L)						
I gr. (n=11)	3.44±0.08	3.58±0.15	3.84±0.12*	3.80±0.12*	4.05±0.15***	4.09±0.15**
II gr.(n=12)	4.36±0.07	4.53±0.06	4.32±0.15	4.47±0.14	4.42±0.17	4.58±0.13
III gr.(n=6)	5.73±0.26	5.42±0.24	4.92±0.29	4.72±0.40	4.56±0.28*	4.68±0.37
TG (mmol/L)						
I gr. (n=11)	1.20±0.19	1.35±0.21	1.37±0.11	1.44±0.11	1.45±0.13	1.44±0.13
II gr.(n=12)	1.42±0.12	1.48±0.21	1.47±0.22	1.43±0.23	1.37±0.18	1.48±0.18
III gr. (n=6)	2.62±0.51	2.66±0.49	2.12±0.44	2.18±0.43	2.17±0.43	2.52±0.45
HDL-C (mmol/L)						
I gr. (n=11)	1.12±0.09	1.16±0.10	1.21±0.08	1.21±0.10	1.33±0.11	1.25±0.09
II gr.(n=12)	1.34±0.09	1.32±0.09	1.37±0.09	1.46±0.09	1.54±0.09	1.42±0.08
III gr. (n=6)	1.42±0.26	1.42±0.26	1.46±0.24	1.46±0.23	1.32±0.23	1.38±0.22
LDL-C (mmol/L)						
I gr. (n=11)	1.79±0.08	1.79±0.12	2.02±0.09	1.94±0.11	2.05±0.09	2.21±0.15
II gr.(n=12)	2.40±0.11	2.56±0.09	2.32±0.12	2.38±0.12	2.33±0.12	2.50±0.09
III gr. (n=6)	3.15±0.14	2.80±0.24	2.50±0.22*	2.27±0.26*	2.27±0.19**	2.15±0.34*
VLDL-C (mmol/L)						
I gr. (n=11)	0.53±0.04	0.63±0.04	0.62±0.05	0.66±0.05	0.67±0.06	0.62±0.10
II gr.(n=12)	0.61±0.03	0.65±0.04	0.63±0.05	0.62±0.04	0.61±0.04	0.65±0.09
III gr. (n=6)	1.17±0.22	1.20±0.21	0.95±0.21	0.98±0.19	0.98±0.19	1.15±0.19

Note: * - P <0.05, ** - P <0.01, and *** - P <0.001 compared to the initial rate.