ORIGINAL RESEARCH

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SIGNS OF POLAR T3 SYNDROME IN YOUNG MEN IN YAKUTIA

The aim of the study was to search for seasonal variations in the levels of thyroid-stimulating hormone (TSH), free triiodothyronine (fT3) and free thyroxine (fT4) in young men in Yakutia, where there are strong changes in climatic parameters in the winter-spring period (from -41.8°C to -0.2°C). Seasonal variations between winter and spring were found for fT3, where in winter its levels were lower – 6.48±0.31 pmol/L than in spring – 6.88±0.1 pmol/L (p=0.005). There were no statistically significant seasonal variations for TSH (U=97; p=0.914) and sv.T4 (U=47; p=0.112). Winter-spring seasonal variations of fT3 detected in this study there are signs of polar T3 syndrome in young men in Yakutia. To search for the causes of the detected seasonal variation, a correlation analysis of the levels of TSH, fT3 and fT4 was carried out depending on daylength and atmospheric air temperature. As a result, a correlation between fT3 and fT4 with the daylight (fT3: R=0.339, p=0.03; fT4: R=-0.346, p=0.01) and with air temperature (fT3: R=0.295, p=0.05; fT4: R=-0.296, p=0.04). No correlations were found with TSH levels (daylight: R=-0.06, p=0.69; air temperature: R=-0.09, p=0.559). Thus, the residents of Yakutia have signs of polar T3 syndrome, which can be associated with both a short light day and low atmospheric temperatures in winter. The results obtained may indicate an increase in the absorption of T3 at the tissue level when exposed to cold.

Keywords: thyroid-stimulating hormone (TSH), free triiodothyronine (fT3), free thyroxine (fT4), Yakutia, polar T3 syndrome.

Introduction. Since 1986, a series of papers has been published on changes in the homeostasis of hormones of the human pituitary-thyroid system during adaptation to a cold climate [1,5,11]. The first studies described seasonal changes in thyroid hormone levels, where a decrease in free triiodothyronine (fT3) levels was recorded after a 42-week residence at McMurdo Station in Antarctica, with significant changes in free thyroxine (fT4) levels and thyroid-stimulating hormone (TSH) was not detected [1,11]. A further study of the kinetics of peripheral levels of T3 showed that with prolonged exposure to cold, the rate of production of fT3 and the rate of removal of fT3 from the blood (clearance) increase, which increases the binding of T3 by various tissues [5]. Identified seasonal changes in the levels of hormones of the pituitary-thyroid system (in winter, the levels of fT3 decrease, the levels of TSH are normal/increase, fT4 are normal/decrease), called "polar T3 syndrome" [5]. Later studies by workers at other polar stations in Antarctica (the Great Wall and Zhongshan) also indicate the presence of seasonal changes in the pituitary-thyroid hormones typical of polar T3 syndrome [6]. In addition, signs of polar T3 syndrome have been identified outside Antarctica, among residents of cold regions, where winter temperatures fall below -40°C, and summer temperatures range from 0°C to +30°C (Finland, Russia) [14,17].

In this regard, the aim of this study is to search seasonal variations in the levels of TSH, fT3 and fT4 in the winter-spring period among the residents of Yakutia, where changes in climatic parameters are observed when the seasons change.

Materials and methods. The research sample comprised 92 Yakut men (with a mean age of 19.91±1.88 years). They presented no health issues at the time of the study, they independently filled out a questionnaire in which they indicated their gender, ethnicity and age. All participants gave written informed consent for participation in the study. Study was approved by the local Biomedical Ethics Committee at the Yakut Scientific Center of Complex Medical Problems, Siberian Branch of the Russian Academy Scientific of Medical Sciences, Yakutsk, Russia (Yakutsk, Protocol No. 16, and 13 December 2014).

Blood samples from the men we studied were carried out from December to May of 2014-2015. For each day of blood sampling, the average atmospheric temperature (°C) and the duration of daylight (hour, minute) were determined. Archived data on weather reports were used to determine the average air temperature (https://www.timeanddate.com). Using an online sunrise/sunset calculator (http://-www.sunrise-and-sunset.com/en/sun) determined the length of daylength.

Venous blood for the study was collected in the morning after an 8-hour fast from all participants. The levels of TSH (μU/ml), fT3 (pmol/L) and fT4 (pmol/L) in fasting blood serum were determined by time-resolution fluoroimmunoassay with using the kits "DELFIA hTSH Ultra", "DELFIA Free Thyroxine", "DELFIA Free Triiodothyronine" (PerkinElmer Inc., USA). The concentration of three hormones in the samples was measured at a wavelength of 450 nm on a VICTOR X5 Multilabel Plate Reader (Perkin Elmer Inc., USA). Normalization of the studied sample by TSH, fT3 and fT4, was carried out using an interquartile (Q1; Q3), so the normalization values were: TSH – 1.62-2.71 μU/ml (n=45), fT3 – 5.96-7.08 pmol/L (n=45), fT4 – 13.2-15.7 pmol/L (n=49).

Statistical analysis. The obtained data were analyzed using Statistica 13.5, a

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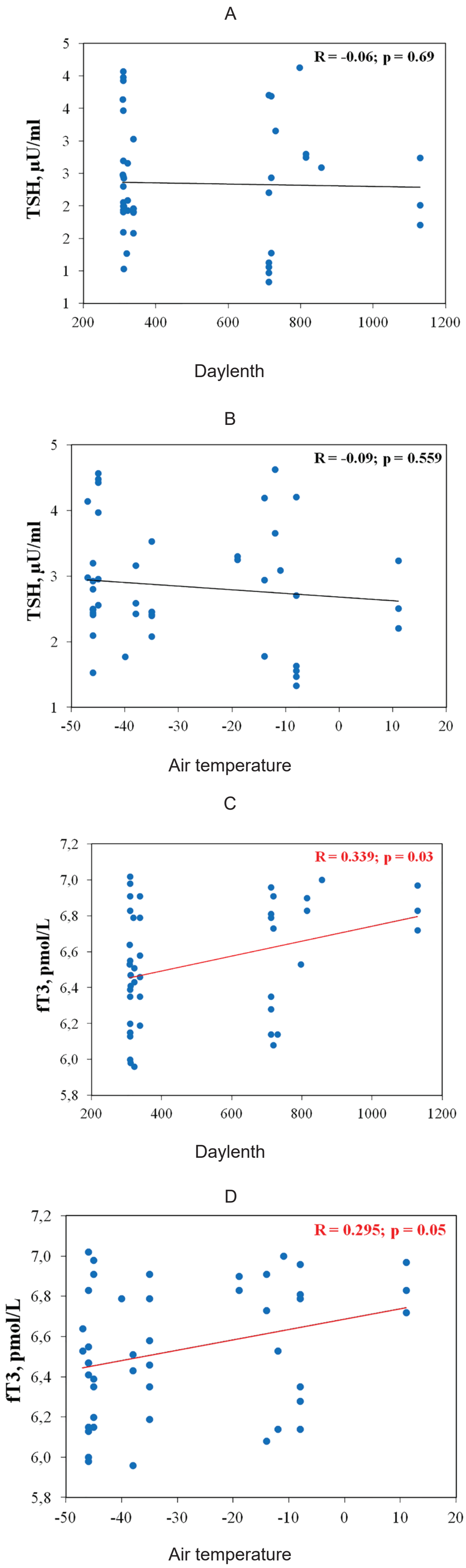
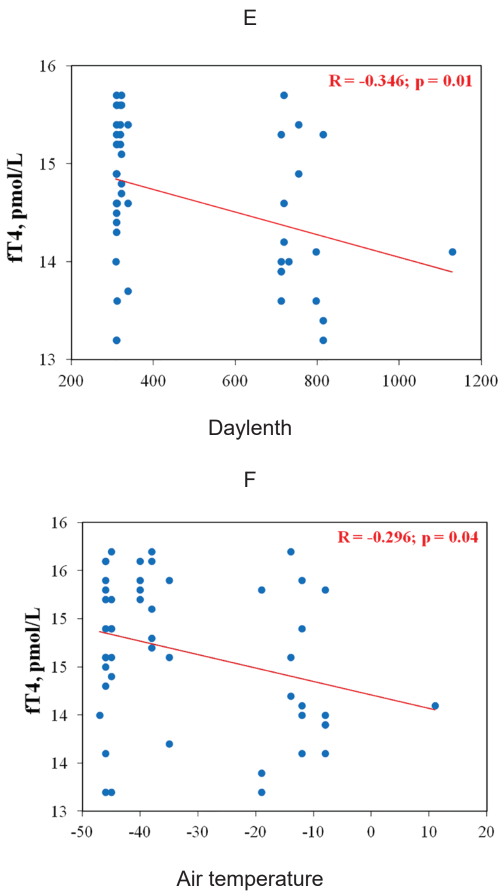
statistical software program (TIBCO Software Inc., Palo Alto, CA, USA). Quantitative results are reported as the mean ± standard deviation. The search for seasonal variations in hormone levels was carried out using the nonparametric Mann-Whitney U-test for small samples (n<100). To determine the dependence of hormone levels on air temperature and the daylight a Spearman correlation analysis was performed. The values of p<0.05 were considered statistically significant.

Results and discussion. *Seasonal variations in TSH, fT3 and fT4 in the "winter-spring" periods.* Comparative analysis of seasonal variations in the levels of hormones TSH, fT3 and fT4 was conducted between the periods "winter" (December-March) and "spring" (April-May) (Table). As a result of this analysis, seasonal changes were detected for fT3 (p=0.005), where in winter its levels were lower (6.48±0.31 pmol/L) than in spring (6.88±0.1 pmol/L). For TSH and fT4 no significant seasonal changes were found.

Our results are consistent with the data of Levy et al., [12] and Leonardo et al., [14] on seasonal variations in the levels of fT3, in residents of central Yakutia, where reduced levels of fT3 were recorded in winter, compared with summer. In addition, seasonal changes in the levels of hormones of the pituitary-thyroid system (TSH, fT4) were also found in children and adolescents from the Arctic regions of Yakutia [13]. Thus, residents of Yakutia have seasonal variations in the hormones of the pituitary-thyroid system, similar to the polar T3 syndrome.

Assessment of the effect of daylength and air temperature on the levels of TSH, fT3 and fT4. It is believed that seasonal changes in the levels of hormones of the pituitary-thyroid system are a consequence of exposure to low atmospheric temperatures, daylength or depression [5], but it is still not known what has a stronger effect on polar T3 syndrome. In this regard, we carried out a correlation analysis of TSH (n=45), fT3 (n=45) and fT4 (n=49) depending on the duration of daylight and air temperature (Figure). At the time of the study, from December to May, the air temperature warmed from -41.8°C to -0.2°C, and daylength increased from 5 hours to 15 hours. Correlation analysis of TSH levels revealed no dependence on daylength and air temperature (Figure A,B). However, we have identified two multidirectional correlations, where with an increase in daylight and an increase in air temperature, the fT3 increased (Figure C,D), and fT4, on the contrary, decreased (Figure E,F). It





Spearman's correlation analysis of TSH (A, B), fT3 (C, D) and fT4 (E, F) with daylight duration and atmospheric air temperature in men

Comparative analysis of seasonal variations in the levels of TSH, fT3 and fT4 between the periods "winter" and "spring"

Hormones	Winter	Spring	U-test	*p*
TSH, µU/ml	2,12±0,29 (n=40)	2,13±0,49 (n=5)	97	0,914
fT3, pmol/L	**6,48±0,31 (n=39)**	**6,88±0,1 (n=6)**	**34**	**0,005**
fT4, pmol/L	14,71±0,73 (n=45)	14±0,95 (n=4)	47	0,116

Note: Statistically significant differences are highlighted in bold (p<0.05)

is known that the thyroid gland produces approximately 80% of T4 and only 20% of T3, while the remaining 80% of T3 comes as a result of conversion from T4, using the type 2 deiodinase enzyme [10]. The results of this correlation analysis show that in winter (short daylight hours and low air temperature) the thyroid gland secretes more T4 than in the warm period, which may indicate the active work of the thyroid gland at this time of year. Thus, we have revealed that the signs of polar T3 syndrome can be affected by both the duration of daylight and negative atmospheric temperatures.

The mechanism of participation of T3 and T4 in nonshivering thermogenesis. The climate of Yakutia is characterized as sharply continental with a fairly long winter, where the air temperatures fall below -40°C. Therefore, in winter, high heat production is required to protect the body from hypothermia. Currently, it is well known that thyroid hormones, together with the adrenergic system, can participate in increasing heat production during nonshivering thermogenesis [4,8,18]. So, in Greenland, Inuit hunters, who were constantly exposed to the cold, had levels of fT3 was lower compared to urban residents who had more comfortable living conditions [19]. Thus, when exposed to cold, brown adipocytes begin to actively absorb fT3 from the blood and additionally convert T4 into T3 with the help of the type 2 deiodinase enzyme. Studies on rats have shown that brown adipose tissue is responsible for about half of the total systemic conversion of T3 from T4 [16], which increase 10-fold under cold exposure [7]. An increase in T3 levels in brown adipocytes enhances the expression of the uncoupling protein thermogenin, thereby increasing the heat production of nonshivering thermogenesis [9,15]. In this regard, we assume that the decrease in the levels of fT3 in the cold season compared with warm periods occurs due to an increase in the absorption of T3 by brown adipocytes in winter, to enhance the thermogenic response of brown adipose tissue in response to cold exposure. This assumption is consistent with the opinion of some authors [12,14] that a decrease in the levels of fT3 in winter (polar T3 syndrome) indicates an increased absorption of T3 at the tissue level during extreme cold. Recent studies have found indirect evidence of brown adipose tissue activity in adult Yakuts in the supraclavicular region [2,3], which may also indicate active uptake of T3 by various tissues, including brown adipocytes in the cold season.

Conclusion. The results of this study show the presence of seasonal variations in the levels of fT3 in the winter-spring period, where since December the levels of fT3 are falling, and since April they begin to rise. At the same time, the levels of fT4 and TSH remain normal. These data indicate the presence of signs of polar T3 syndrome in young men in the climatic conditions of central Yakutia. The search for the causes of the revealed seasonal variations showed that at the levels of fT3 can affect both the daylength and the air temperature. A decrease in the levels of fT3 in the cold season compared to warm periods may indicate an increase in the absorption of T3 at the tissue level.

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ASSESSMENT OF THE RELATIONSHIP OF LIPID METABOLISM INDICATORS AND PULMONARY HYPERTENSION IN THE INITIAL PERIODS OF MYOCARDIAL INFARCTION IN MEN UNDER 60 YEARS OLD

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Pulmonary hypertension (PH) is an understudied but significant complication of myocardial infarction (MI). Currently, there are no diagnostic algorithms that can predict the development of PH in the setting of myocardial infarction, which requires the development of prediction models based on the results of routine examination, for example, lipid profile. The purpose of the research was to study the parameters of lipid metabolism in men with PH that developed against the background of MI and their impact on the risk of developing PH. The results of examination of men aged 32-60 years with verified MI were studied. According to the level of mean pulmonary artery pressure (MPAP) determined by echocardiography, patients were divided into two groups: the study group (with a MPAP level of more than 20 mm Hg at the end of the third week of MI) and the comparison group (with a normal MPAP level at the end of the third week of MI). The studied indicators were compared based on the Mann-Whitney, Wilcoxon, and Chi-square tests; correlations were performed using the Spearman method. It was found that patients in the study group had lower levels of the atherogenic coefficient (AC) and the total cholesterol/high-density lipoprotein (TC/HDL) index at the end of the third week of MI. Levels of triglycerides (TG) < 1.3 mmol/l and very low density lipoprotein (VLDL) ≥ 1.2 mmol/l, TC/HDL indices < 6.0 and LDL/HDL < 3.2 in the first 48 hours, LDL <2.4 mmol/l, AC value <5.0, TC/HDL indices <6.0 and LDL/HDL <3.2 at the end of the third week of MI influence the risk of developing PH in the subacute period of MI. Correlations have also been established between the level of MPAP and lipid profile parameters. It is advisable to use the obtained results when developing a model for predicting the development of PH against the background of MI.

Keywords: pulmonary hypertension, myocardial infarction, lipid metabolism, mean pulmonary artery pressure, heart failure, men, young and middle age.

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Introduction. Diseases of the cardiovascular system currently dominate the structure of causes of mortality throughout the world, and myocardial infarction (MI) remains one of the most significant among them [12]. The prognosis of a patient with MI largely depends on the presence and severity of complications, among which it is worth highlighting pulmonary hypertension (PH) [1]. This syndrome is characterized by a predominantly asymptomatic course, which leads to its detection only at the stage of development of irreversible changes in pulmonary hemodynamics, aggravating the course of MI and contributing to an increase in mortality [17]. Timely diagnosis of PH in MI will allow identifying patients at high risk of its development for dynamic monitoring and timely implementation of preventive and therapeutic measures. It is advisable to base forecasting models on routine diagnostic methods that do not require additional time and economic