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ARCTIC MEDICINE

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DETERMINATION OF VITAMIN D CONCENTRATION OF 25(OH) IN THE WORKING-AGE POPULATION OF THE NORTHERN REGION

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The study examined working-age population of the North region to determine 25 (OH) vitamin D concentrations and compared insufficient subjects (Group 1) with those having the proper/optimal vitamin D concentration (Group 2) in terms of main indicators of physical development, cardiovascular system, biochemical and trace element picture.

Material and Methods: fifty-five men of working age (mean age was 37.4±0.5 yr.) all Caucasians residing in the territory of Magadan region participated in the research. We used photometric, immunochemiluminescent and spectrometric methods of investigation, as well as standard cardiovascular and anthropometric measurements. Study Results: 42% (Group 1) tested low for vitamin D while 58% (Group 2) had the proper vitamin amounts. Group 1 was up to 78% made up of high body mass index men versus 40% of subjects exceeding standard range of this index in Group 2. Cardiovascular system and circulation values tended to be increasingly stressed and high thyroid-stimulating hormone indicated the development of preclinical hypothyroid pathology with Group 1 examinees. They were more atherogenic in lipid pictures in comparison with Group 2 northerners who showed a shift towards healthier lipid profiles. Moreover, vitamin D deficient subjects proved to also lack vitamin B12 and were low in trace elements.

Conclusion: Subjective vitamin D deficits develop disorders in physical development, cardiovascular system, as well as biochemical and trace element profiles. Our study can be applied for making recommendations on correcting vitamin D deficiency/insufficiency in residents of Russia's northeast.

Keywords: men of working age, 25 (OH) vitamin D, North, physical development, cardiovascular system, biochemical picture, trace elements.

Introduction. Vitamin D insufficiency has become a pandemic health problem [24] since it is common in a third of the world's population, even in Earth's tropical and subtropical regions [16]. It can be invasively assessed in blood serum 25-hydroxyvitamin D (25(OH) vitamin D) concentration [27]. In addition to significantly influencing calcium and phosphorus metabolism, thereby bone health and muscle strength, vitamin D deficiency has been recently reported to develop non-skeletal disorders like cardiovascular [20] and autoimmune diseases, cancers [19], higher blood pressure, depression, as well as overall mortality [34]. Some authors have investigated the relationship between low blood 25(OH) vitamin D and chronic diseases, including insulin resistance [21] and type 2 diabetes mellitus [18].

Vitamin D deficit is a variable which the patient's mineral picture can also be referred to. Therefore, vitamin D control is crucial for the body mineral imbalance management [37]. Trace elements are known to be involved in metabolic activities. They promote vascular tone, nervous and immune functioning at the enzymatic level. Unlike blood or urine, hair is known to constantly accumulate chemicals as the hair shaft grows and is supplied with blood [36]. Therefore, hair elemental composition reflects longer exposure to the chemicals owing to the hair biomonitoring abilities to keep past changes in metabolism as well as environmental effects [1,7,13].

The role of vitamin D in maintaining the proper blood calcium and phosphorus levels has been commonly reported [3] for it ensures bone tissue mineralization and enhances the re-absorption of calcium in kidneys. Extremely low levels of vitamin D can provoke improper calcium and phosphate metabolism, which causes bone tissue impairment. Insufficient absorption of calcium in the intestine results in accelerated release of calcium from bones, which decreases the bone density and increases the risk of fractures [8]. Vitamin D deficiency is often accompanied by shortage of thyroid-specific elements such as cobalt, iron, magnesium, selenium, copper, and zinc, which can be seen under the goiter endemic conditions. The so called northern deficit in essential macro- and microelements owing to the biogeochemistry of the region, as well as poor soils and weakly mineralized drinking waters can develop insufficient absorption of the vitamin, even being taken as a supplement. The specific light regime of the

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northern territories suggests a long dark period in winters, which inhibits the vitamin D absorption and leads to its chronic deficiency.

Thus, hair mineral analysis is a non-invasive, painless, and easy to collect method for determining biomarkers, which requires no special storage conditions [39]. Sampling the hair should be also considered as an indicator of nutrition deficiencies [11]. This study was the first investigation performed in Magadan region to comparatively assess the main indicators of physical development, cardiovascular system, biochemical and trace element pictures in Russia’s far north residents with insufficiency or the optimal concentration of vitamin D.

Materials and Methods. Fifty-five male residents (mean age was 37.4 ± 0.5 yr) of Magadan region, Caucasians by origin, participated in the survey within the framework of psychophysiological monitoring of people of the working age under conditions of the North-East of Russia entitled “Arctic. Man. Adaptation” carried out with the Arktika SRC, FEB RAS (Magadan) as part of state assignment. Blood serum samples were taken to study 25 (OH) vitamin D with the Unicel DXi 800 automated immunochemical analyzer (Beckman Coulter, USA) using ACCESS-ELISA technology on submicron paramagnetic particles as a solid phase and enzymatically enhanced chemiluminescence as a detection method.

In this research, insufficient and optimal blood serum 25 (OH) vitamin D concentration values were taken to be less or more than 50 nmol/L [5], respectively, in accordance with the criteria of the Clinical Recommendations of the Russian Association of Endocrinologists (2016). Further, two groups of subjects were formed: Group 1 were subjects who demonstrated a deficiency of 25 (OH) vitamin D (n=23, 42%) and Group 2 were those with the optimal amounts of 25 (OH) vitamin D (n=32, 58%).

The participants’ anthropometric characteristics, body length and body mass, were measured to calculate the body mass index (BMI, kg/m^2) was calculated. Using the AIST software package of the Diamant-AIST body impedance analyzer (Diamant, Russia), the total fat content (in % of the body mass) was determined. Systolic (BP_S, mmHg) and diastolic (BP_D, mmHg) blood pressure and heart rate (HR, beat p min) were also measured on the forearm area with the Nessei DS-1862 automated tonometer (Japan).

The variables for total cholesterol (TChol, mmol/L), triglycerides (TG, mmol/L), high-density lipoprotein cholesterol (HDL, mmol/L) and low-density lipoprotein cholesterol (LDL, mmol/L) were determined by colorimetric photometric method using AU 680 (Beckman Coulter, USA). Dyslipidemia of the analyzed variables was determined based on the criteria of the Russian Recommendations of the VII Revision of 2020 [4] and based on the Report of NCEP experts [30].

The amounts of vitamin B_{12} (pmol/L) and thyroid-stimulating hormone (TSH, mcME/mL) were determined with the immunochemiluminescent method using the IMMULITE 2000 XPI Siemens healthcare diagnostics immunochemical analyzer (USA - Germany).

Hair samples were cut from the occipital part of the head to study and analyse amounts of micro- and macroelements (ME): Co, Cr, Fe, I, Mg, Mn, Se, V, Zn, Cu, P, and Ca. This analysis was performed with the laboratory of Micronutrients LLC (Moscow) using the NexION 300 ICP-MS device (Perkin Elmer, Shelton, CT, USA) with the inductively coupled plasma spectrometric method.

The study was conducted in accordance with the ethical principles of the Declaration of Helsinki for medical research involving human subjects, including research on identifiable human material and data (2013) [40], with the informed consent of voluntary participants. The study protocol was approved by the Bioethics Commission of the IBPN, FEB RAS (No. 001/019 dated 29.03.2019).

The results of the studies were statistically processed using the Statistica 7.0 software package. The distribution of measured variables was tested for normality using the Shapiro-Wilk test. The results of parametric processing methods were presented as the mean value (M) and its error (±m). The statistical significance of differences was determined using the Student’s test *t*. The critical level of significance (p) was assumed to be 0.05; 0.01; 0.001 [2].

Results. The results in Table 1 show subjective variables of physical development, cardiovascular system, and biochemical picture when insufficient (Group 1) and optimal (Group 2) vitamin D examinees are compared. The data indicate statistically significant differences in 17 of the 26 analyzed indicators. Low 25 (OH) vitamin D participants, regardless of their ages, exhibited significantly higher variables of body mass, total body fat, body mass index, systolic and diastolic blood pressure, and heart rate. Biochemical picture analysis revealed higher amounts of B_{12} and D vitamins in Group 2 individuals, with significantly lower values of thyroid-stimulating hormone, total cholesterol, low-density lipoprotein cholesterol, and triglycerides observed in this group. Table 2 presents microelement pictures in subjects with insufficient and the optimal vitamin D concentrations. The results indicate more pronounced trace element deficits observed in Group 1. Figure 1 shows correlation patterns of the studied indices for physical development, cardiovascular system, biochemical and trace element pictures, which are seen to differ depending on the body vitamin D supply.

Discussion. Data in Table 1 show significantly higher body weight, total body fat amount, and body mass index exhibited by insufficient vitamin D subjects. Body mass index (BMI) is known to be the world’s recommended indicator for overweight and obesity. In addition, BMI specifies nutritional status and, according to some authors, strongly correlates with the total body fat and risks for developing metabolic and cardiovascular diseases [32]. The relationship between BMI and total body fat is however reported to not be strong enough to accurately assess the obesity in a particular case since the use of BMI in obesity assessment does not consider body composition [38]. Thus, the total body fat value is a true risk factor for cardiometabolic health and human life expectancy, while the use of BMI is rather approximate and insufficient [32].

Total body fat content has a potential advantage in more accurate identifying the metabolic phenotype than BMI [22]. Group 1 of those with vitamin D deficiency tended to be mostly made up with men with a BMI exceeding the range for normal body mass (25 kg/m^2) which is more common in insufficient (up to 78%) than in optimal vitamin D examinees (40%). That was also investigated by T.L. Karonova who has reported that patients with normal BMI had a higher level of 25 (OH) vitamin D than overweight and obese patients (52.5 ± 2.8 and 44.8 ± 2.0 nmol/L, p<0.05) [26]. Obesity results in decreased blood serum vitamin D concentration [10]. It worsens bioavailability of vitamin D from food and impairs its synthesis in the skin [26]. Thus, we identified Group 2 of 25 (OH) vitamin D deficit subjects as having worse physical development owing to the obtained somatometric variables.

As seen from Table 2, we found 49% of volunteers to be low in Vanadium, which can be accompanied by decreased cholesterol and increased levels of triglycerides, liver lipids and phospholipids in blood plasma, as well as higher hematocrit, which may cause the risk for atherosclerosis and diabetes mellitus. Table 2 shows significant differences in chromium amounts between the two groups. Chromium imbalance can develop atherosclerosis, obesity, and worsen thyroid generative function. In addition, it is a mediator of the insulin signal in insulin-dependent tissues. Since that, when being low, chromium is consistently accompanied by impaired glucose and lipid metabolism and decreased insulin sensitivity [31].

By cardiovascular system analysis, we identified insufficient blood serum vitamin D subjects as tension in the circulatory system activity and significantly higher systolic and diastolic blood pressure which have been reported to correlate with lowered 25 (OH) vitamin D concentrations [35].

By biochemical study of lipid metabolism, we revealed significantly higher levels of total cholesterol, low-density lipoproteins and triglycerides with Group 1 subjects with no differences observed about high-density lipoproteins. A high frequency for lipid profile disorders was also seen in insufficient blood serum vitamin D subjects who demonstrated hypertriglyceridemia (38% of cases), hypercholesterolemia (69%), increased LDL (95%) versus those of Group 2 who showed hypertriglyceridemia in 10%, hypercholesterolemia in 53% and increased LDL in 75%.

Thus, during this study, a more atherogenic lipid picture was typical for insufficient vitamin D Group 1 examinees whereas the optimal vitamin D concentration subjects reported a healthier lipid profile.

Vitamin B_{12} deficiency is a worldwide public health concern, especially in developing countries, where it affects the population of all ages [25]. In developed countries, vitamin B_{12} deficiency is most common in the elderly, however the prevalence in younger people is higher than previously thought [25]. As a result, a wide range of neurological, hematological and neuropsychiatric disorders can happen [23]. In addition, the vitamin deficiency indirectly effects on cardiovascular system [15]. The blood serum vitamin B_{12} concentration is considered to be deficient or low when being below 200 pg/mL (147 pmol/L) or below 400 pg/mL (296 pmol/L), respectively [12]. Based on these criteria, insufficient vitamin D Group 1 participants were diagnosed with the deep B_{12} deficiency in 25% of cases, 69% of them were low in the vitamin, and 6% only showed its optimal level.

Subjective B_{12} variables within Group 2 suggested that the vitamin deficiency was common in 12% of the sample, 63% were considered as insufficient while 25% were defined as the optimal level. Low vitamin B_{12} levels are associated with high body fats in healthy adults who are not obese [9], which complies with our studies owing to higher BMI and total fat amounts in individuals with significantly low vitamin B_{12} values. Therefore, the data indicated that Group 1 participants with vitamin D deficiency tended to be low in vitamin B_{12} as well.

The study revealed cobalt deficiency as a common north-related trace element picture in 78% of the examinees which causes impairment in synthesis of vitamin B_{12}, as well as endemic weakness in thyroid functioning (hypothyroidism), develops cardiovascular diseases, anemia, central nervous system disorders and depression.

Thyroid function is mostly monitored by measuring thyroid-stimulating hormone (TSH). Subclinical hypothyroidism is defined as the TSH level above the reference ranges while the level of thyroid hormones remains within the normal range [29].

Our results suggested that TSH of both examined groups were significantly lower than currently used world's reference upper values being equal to as high as 4.2 mcME/L [17], but for Group 1 with vitamin D deficiency, the average TSH values highly exceeded the threshold of 2.5 mcME/L, which was proposed by the NACB

Table 1

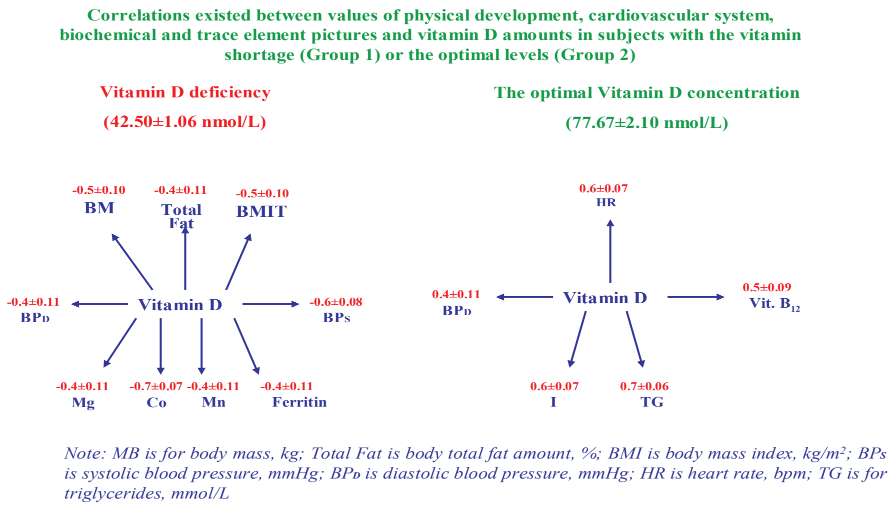
Indicators of physical development, cardiovascular system, biochemical pictures in subjects with insufficient and optimal amounts of vitamin D

Indicator	Insufficient Vitamin D	Optimal Vitamin D	Levels of Significance of Differences
Age, yr	37.2±1.2	37.5±1.0	p=0.82
Body Mass, kg	86.6±1.5	82.7±1.2	p<0.05
Total Fat Amount, %	20.2±0.8	17.7±0.7	p<0.05
BMI, kg/m^2	26.8±0.4	25.6±0.3	p<0.01
BPS, mmHg	128.0±1.8	122.4±1.7	p<0.05
BPD, mmHg	84.3±1.9	78.1±1.6	p<0.05
HR, bpm	69.1±2.3	62.7±1.8	p<0.05
Vit B12, pmol/L	189.80±9.71	251.10±18.30	p<0.05
Vit D, nmol/L	42.50±1.06	77.67±2.10	p<0.001
TSH, mcME/mL	2.75±0.15	2.31±0.10	p<0.05
Cholesterol, mmol/L	6.25±0.19	5.62±0.14	p<0.01
HDL, mmol/L	1.41±0.05	1.42±0.07	p=0.91
LDL, mmol/L	4.26±0.16	3.73±0.18	p<0.05
TG, mmol/L	1.80±0.19	1.16±0.12	p<0.01

Table 2

Microelement pictures in subjects with insufficient and optimal amounts of vitamin D

Indicator	Insufficient Vitamin D	Optimal Vitamin D	Level of Significance of Differences	Reference Values [6]
Co, mc/g	0.008±0.001	0.011±0.001	p<0.01	0.004-0.3 mc/g
Cr, mc/g	0.46±0.04	0.40±0.03	p=0.23	0.04-1 mc/g
Fe, mc/g	29.58±4.47	18.13±1.57	p<0.05	7-40 mc/g
I, mc/g	0.22±0.02	0.56±0.05	p<0.001	0.15-10 mc/g
Mg, mc/g	31.20±1.20	39.64±3.60	p<0.05	20-200 mc/g
Mn, mc/g	0.38±0.03	0.46±0.03	p=0.07	0.15-2 mc/g
Se, mc/g	0.50±0.03	0.61±0.05	p<0.05	0.25-2 mc/g
V, mc/g	0.03±0.00	0.02±0.00	p=0.10	0.005-0.1 mc/g
Ca, mc/g	280.0±26.6	301.8±27.0	p=0.54	200-2000 mc/g
Zn mc/g	181.56±13.97	182.57±11.88	p=0.96	125-400 mc/g
Cu, mc/g	12.06±0.73	12.26±0.99	p=0.84	9-40 mc/g
P, mc/g	172.8±7.8	189.6±6.8	p=0.72	120-200 mc/g



Analysis of correlations existed between indices of physical development, cardiovascular system, biochemical and trace element pictures in insufficient and optimal vitamin D subjects

for determining preclinical hypothyroidism [14]. In this study we determined the relationship of increased TSH levels with subjective high serum lipids and risks for atherosclerosis [33], which was obviously exhibited by Group 1 lipid picture. In addition, Iodine deficiency demonstrated by vitamin D insufficient subjects can develop hypothyroidism, cardiovascular and reproductive impairments, physical and mental problems, worsened cognitive functions, especially under conditions of the previously observed endemic goiter.

Table 2 shows mineral pictures of the surveyed participants with significant differences in bioelement amounts through both groups. Group 1 subjects exhibited imbalanced magnesium and manganese [28], vanadium and selenium [29], known as important in metabolism of carbohydrates and fats.

By correlation analysis (Fig. 1), we revealed stronger negative intersystem correlations typical for insufficient vitamin D subjects’ physical development, cardiovascular system, as well as biochemical and trace element profile. The negative correlations that exist with deficient chemicals can indicate the dysregulation in the relationships. The less stable a system is the more correlations can develop within it. Strong correlations of magnesium and manganese with deficient vitamin D can indicate the risk for neurosis-like conditions, impaired glucose metabolism, osteodystrophy, and bone fragility, especially with low calcium and phosphorus amounts typical for this group. For northern men with the optimal blood vitamin D concentration, a different picture of intersystem correlations could be seen, with no relationships with indicators of physical development apparently owing to subjective healthier values of BMI and total body fat in Group 2. Negative correlations occurred between 25(OH) D and BMI (r=-0.17, p=0.03) were also reported by T.L. Karonova [26]. Furthermore, the direct correlations with the indicators of systolic and diastolic blood pressure, the concentration of vitamin B_{12}, the level of blood triglycerides, and the body iodine concentration were observed with the examinees of this group.

Conclusion. Thus, by comparative analysis, we determined significant differences in the surveyed northern men’s functional status, as well as their biochemical and trace element pictures depending on vitamin D levels. Group 1 of those tested low for the blood vitamin D levels exhibited significantly high BMI and total body fat values, which can be considered as a sign of deterioration in physical development. A more atherogenic lipid picture was typical for this group, and dyslipidemia in LDL and TChol values, as well as triglyceride concentration was more common in Group 1 of low 25(OH) vitamin D examinees. Group 2 of northerners tested for the optimal vitamin D concentration demonstrated healthier lipid pictures.

The study confirmed that the deficiency group reported deficit in both D and B_{12} vitamins. By cardiovascular analysis, we could see insufficient blood serum vitamin D subjects having significantly higher (vs. the other group) systolic and diastolic blood pressure, which indicated circulatory system tension, as well as higher thyroid-stimulating hormone values, which we considered to be Group 1 subjects’ symptom of the developing preclinical hypothyroidism.

In the surveys, subjective vitamin D, depending upon its levels, differently correlated with the values of physical development, cardiovascular system, as well as indicators of biochemical and trace element pictures. By intersystem analysis we determined that low vitamin D concentration caused dysregulation with examinees diagnosed with its deficiency since they exhibited strongly negative relationships.

We consider the results of this survey to be useful for assessment of either vitamin D supply or other functional parametric values as predictive markers of vitamin D deficiency that do not require invasive and costly research methods. Based on the research, specific recommendations can be created for people diagnosed with vitamin D deficiency, as well as for those working shifts under extremes of the northeast of Russia.

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