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BRIEF MESSAGES

Relationship between Dehydroepiandrosterone-Sulfate, Testosterone, Thyroid Hormones, Insulin, and Cortisol in Indigenous Men and Women among Representatives of the Indigenous and Newcomer Population of the Yamalo-Nenets Autonomous Okrug

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Abstract—Using Spearman's rank correlation we studied the correlations between the serum dehydroepiandrosterone-sulfate (DHEA-S) concentration and the concentration of testosterone, thyroid-stimulating hormone, thyroxine, triiodothyronine, insulin, and cortisol in the indigenous and newcomer population of the Yamalo-Nenets Autonomous Okrug. A positive correlation was found between the DHEA-S concentration and testosterone in indigenous women and newcomers. A stronger correlation was found in the group of newcomer women. In indigenous men, DHEA-S was positively correlated with cortisol. The newcomer men showed a positive correlation between DHEA-S and thyroid-stimulating hormone. No correlations were found between the concentration of DHEA-S with insulin, thyroxine, and triiodothyronine in any of the examined groups.

Keywords: dehydroepiandrosterone sulfate, testosterone, thyroid hormones, insulin and cortisol, village residents of the Yamalo-Nenets Autonomous Okrug

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INTRODUCTION

Dehydroepiandrosterone sulfate (DHEA-S) is a particular hormone that has attracted increased interest in recent decades. Based on experimental studies and clinical observations, DHEA-S in the form of dehydroepiandrosterone (DHEA) is used to treat various diseases. Epidemiological studies have found an association between low levels of DHEA-S and the occurrence of cardiovascular disease. In addition, anti-diabetic, anti-carcinogenic, and anti-atherosclerotic properties of the hormone have been demonstrated. DHEA-S prevents obesity, the development of osteoporosis, and supports memory [1]. DHEA-S and DHEA are the most commonly used steroids in humans. Despite a large number of studies, the biological significance of high concentrations of DHEA-S and the specific mechanisms of action of DHEA and DHEA-S remain a mystery, as well as a significant decrease in DHEA-S with age [2]. The level of DHEA-S and DHEA varies widely in healthy people of the same age, but with different heredity [3], lead a different lifestyle, or are under the influence of prolonged stress [4, 5]. One of the possible approaches to understanding the role of DHEA-S is the analysis of correlations between endocrine parameters in representatives of different population groups (influence of hereditary factors) and/or those under the influence of various environmental factors (environmental factors). The aim of this study was to study the correlation between DHEA-S and the concentration of testosterone, thyroid-stimulating hormone (TSH), thyroxine (T4), triiodothyronine (T3), insulin, and cortisol in native and new residents of the Yamalo-Nenets Autonomous Okrug.

METHODOLOGY

The study was carried out on 240 volunteers (men and women), representatives of the indigenous and alien population of the Yamalo-Nenets Autonomous Okrug. Blood samples were taken from practically healthy subjects at the time of the study. The study included women (n = 101; age 41.0 ± 1.0 years) and men (n = 34; 34.2 ± 2.2 years) of an indigenous nationality (Forest and Tundra Nenets), as well as representatives of the Caucasoid population of the settlements of the Yamalo-Nenets Autonomous Okrug: 66 women (age 42.1 ± 1.3 years) and 39 men (44.4 ± 1.9 years). Blood was taken from the cubital vein on an empty stomach after a 10–12-h period of overnight fasting by venipuncture into a BD Vacutainer special sterile vacuum system. In the examined patients, the

Table 1. Correlations of dehydroepiandrosterone sulfate (DHEA-S) with testosterone, thyroid hormones, insulin, and cortisol in indigenous and newcomers of the Yamalo-Nenets Autonomous Okrug

Indicators	Spearman's rank correlation coefficients (*rs*) with DHEA-S	*p*-level
Indigenous women ($n = 101$)		
Testosterone	0.325	0.01
T4	0.009	0.05
TSH	0.190	0.05
T3	0.026	0.05
Insulin	0.093	0.05
Cortisol	0.025	0.05
Newcomer women ($n = 66$)		
Testosterone	0.424	0.001
T4	0.143	0.05
TSH	–0.077	0.05
T3	–0.046	0.05
Insulin	0.038	0.05
Cortisol	–0.038	0.05
Indigenous men ($n = 34$)		
Testosterone	0.309	0.05
T4	0.036	0.05
TSH	0.092	0.05
T3	0.114	0.05
Insulin	–0.069	0.05
Cortisol	0.525	0.01
Newcomer men ($n = 39$)		
Testosterone	–0.238	0.05
TSH	0.331	0.01
T4	–0.089	0.05
T3	–0.154	0.05
Insulin	–0.001	0.05
Cortisol	–0.041	0.05

T4—thyroxine, TSH—thyroid-stimulating hormone, T3—triiodothyronine. The table shows the absolute values *rs*.

content of TSH, T4, T3, insulin, cortisol, DHEA-S, and testosterone was determined in the blood serum using Alkor Bio (Russia) and Monobind Inc. (United States) kits. The optical density was measured on an ELISA Statfax 2100 microplate photometer for (Awareness Technology, United States). The described methods were used earlier in [6, 7].

The linear relationship between quantitative traits was assessed using the Spearman rank correlation coefficient (*rs*). Critical level of significance (*p*) was taken equal to 0.05. For statistically significant differences the exact value *p* is shown in Table 1.

RESULTS AND DISCUSSION

In previous studies, we presented the endocrine parameters of blood serum in residents of the indigenous (forest and tundra Nenets) and alien population living in the district settlements of the Yamalo-Nenets Autonomous Okrug. The state of the thyroid link (TSH, T3, T4), the concentration of insulin in the blood serum, as well as steroid hormones (cortisol, DHEA-S, and testosterone) were determined. It was shown that such endocrine indicators as TSH, T4, and cortisol in northern women are within the reference norm values. A distinctive feature of the endocrine spectrum of blood in women in the North was an

increased level of T3, and, most importantly, an increase in insulin against a background of a decrease in testosterone levels. We have not found differences in the content of cortisol and T4 between groups of men. In addition, there were no statistically significant differences in the content of TSH, T3, testosterone, and DHEA-S [6, 7].

The aim of this study was to study the correlations between the relationship between DHEA-S and the concentration of testosterone, thyroid hormones, insulin, and cortisol in the blood serum of native and alien residents of the Yamalo-Nenets Autonomous Okrug. Spearman's rank correlation coefficients and the level of statistical significance of the revealed correlations are given in Table 1.

From the data in Table 1 it follows that in the groups of women of the indigenous nationality and aliens, DHEA-S positively correlated with testosterone. Moreover, a stronger correlation was found in the group of newcomer women ($rs = 0.424$; $p < 0.001$). It is known from the literature that DHEA-S positively correlates with testosterone in women, regardless of the use of combined hormonal contraceptives. So, in women who received DHEA 50 mg/day for 6 months, testosterone levels increased along with an increase in DHEA-S. Continuation of therapy up to 1 year led to some decrease in blood levels of both testosterone and DHEA-S. In the group of men who received similar DHEA therapy, there was only an increase in the level of DHEA-S in the first half of the year and a slight decrease in its level in the second half of the year, in the absence of statistically significant changes in testosterone [8].

The finding of a strong correlation between DHEA-S and testosterone in women can be explained by the fact that DHEA-S, which is a weak androgen, increases its androgenic activity by transforming under the influence of liver steroid sulfatase into DHEA, and then into Δ4-androstenedione, which undergoes conversion in peripheral tissues to testosterone. In women, up to 50% of circulating testosterone is formed in this way [9].

We have not found a correlation between DHEA-S and testosterone in both native and alien men. This has been confirmed by E.I. Georgiadis et al. [10], using a survey of 92 healthy young men. According to the authors, although common steroidogenic pathways can lead to androgen synthesis in both the adrenal glands and the testes, different factors influence the regulation of steroid production in these glands [10].

Cortisol and DHEA-S are the main hormones of the adrenal cortex. Cortisol secretion is the result of steroidogenic activity in the zona fasciculata, while DHEA-S and DHEA are secreted in the zona reticularis. The secretion of DHEA-S by the adrenal glands is episodic and follows a diurnal rhythm similar to that of cortisol under the action of the corticotropin-releasing factor and adrenocorticotropic hormone (ACTH) [9, 11]. According to their biological action, DHEA and DHEA-S are considered as antagonists of glucocorticoid hormones. It is generally accepted that in the process of aging, the predominance of the catabolic effects of cortisol increases with a simultaneous decrease in the anabolic effect of DHEA-S [12]. The positive correlation between DHEA-S and cortisol revealed by us ($rs = 0.525$; $p < 0.01$) in indigenous men, despite their functional differences, confirms the possible similarity of the response to the influence of individual regulatory factors, in particular, stimulation of the production of these hormones by the adrenal cortex under the influence of ACTH.

Another ethnicity-related feature was the positive correlation of DHEA-S with thyroid-stimulating hormone ($rs = 0.331$; $p < 0.01$) in the group of male representatives of the newcomer population. A similar positive correlation of DHEA-S with TSH was found in a Czech population of healthy men [13].

CONCLUSIONS

(1) A positive correlation of DHEA-S with testosterone was found in the group of women of indigenous nationality and aliens. A stronger correlation was found in the group of newcomers.

(2) In indigenous men, DHEA-S was positively correlated with cortisol.

(3) In alien men, a correlation of DHEA-S with TSH was revealed.

(4) None of the examined groups showed correlations between DHEA-S and insulin, T4 and T3.

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COMPLIANCE WITH ETHICAL STANDARDS

All studies were conducted in accordance with the principles of biomedical ethics, formulated in the Declaration of Helsinki 1964 and its subsequent updates and approved by the local ethics committee Federal Research Center for Fundamental and Translational Medicine (Novosibirsk).

INFORMED CONSENT

Each participant in the study provided a voluntary written informed consent signed by him after explaining to him the potential risks and benefits, as well as the nature of the upcoming study.

CONFLICT OF INTEREST

The authors declare the absence of an obvious and potential conflict of interest related to the publication of this article.

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