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Assessment of Androgen Status in Female Patients with Chronic Obstructive Pulmonary Disease.

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ABSTRACT

The article presents the data about androgen status of female patients with moderate and severe chronic obstructive pulmonary disease. The relations between the course of COPD and hormonal levels were analyzed. The obtained data present evidence that the level of androgens such as testosterone and DHEA-S in female patients, are predictors of worsening of COPD.

Keywords: Chronic obstructive pulmonary disease, androgen status, women.

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INTRODUTION

The endocrine glands take active part in human organism adaptation to various physiological and pathological stimuli. Many researchers noted the close relationships between the endocrine system dysfunction and the course and prognosis of chronic obstructive pulmonary disease; and the modern concepts of COPD pathogenesis created the prerequisites for detailed exploration of this link to discover novel options for prevention and treatment of the disease[1, 3, 11].

The idea of assessing the androgen status of female COPD patients seemed to be interesting. By the hypoandrogenic state in women we mean the decreased production of not only ovarian but adrenal androgens as well.The mechanisms responsible for the age-dependent decline of testosterone level in females include the lowering of adrenal DHEA production[4] and increase of specific activity of adipose tissue aromatases.

DHEA is the main precursor of human steroid sex hormones. DHEA-S is considered a circulating depot for DHEA regeneration. DHEA has weak androgenic effect and is a precursor in the system of synthesis of sex steroid hormones: androgens – testosterone and androstendione, and estrogens – estradiol and estrone. In peripheral tissues, the hormone may be converted into potent androgens – testosterone and dihydrotestosterone. Estrone is formed from DHEA-sulphate in the liver and adipose tissue. It is believed that the decline in DHEA and DHEA-S levels and high cortisol/DHEA or cortisol/DHEA-S ratios create disbalance between protein synthesis and the dominance of catabolism over anabolism [5].The main risk factors causing the lowering of serum DHEA are aging [6, 8, 9] and the severe obstruction of airways, hypoxemia and hypercapnia. Dehydroepiandrosterone (DHEA) is considered as an important immune modulation and anti-inflammatory hormone. Despite the persistent interest in therapy with DHEA, there is limited knowledge of its effect on COPD pathogenesis. Adrenal androgens constitute a significant part (more than 50 %) of circulating androgens in reproductive age females. After menopause, the adrenals remain the primary reserve of androgens and estrogens, and the suppression of adrenal function with glucocorticoid therapy leads to lowering of androstendione, testosterone and estrone production. Moreover, the activity of androgens and estrogens formed from DHEA by enzymes expressed in peripheral target tissues, depends on DHEA concentration.All of the above form the basis for deeper assessment of androgen production in COPD as well as for comprehensive investigation of this disorder.

The aim of this study is to assess the production of androgens and their relationships with the pathological activity in COPD patients and to substantiate the choice of treatment modality [2, 11].

MATERIALS AND METHODS

Female patients with moderate and severe COPD stage II and III were included in the study.COPD diagnostics, stage and severity determination was conducted according to the international program “COPD Global Initiative (GOLD), 2017”, National pulmonology guidelines and International Classification of Diseases, 10th revision (ICD-10) (WHO, Geneva, 1992) [7].The signed informed consent form was obtained from each enrolled patient. The controlled study of disease clinical manifestations and recording of subjective and objective parameters of internal organs and systems examination was done on Day 1 of hospitalization and on Days 13–14 of treatment.During the study, the clinical symptoms were evaluated using point system.The spirometry was performed with the measurement of FEV_1, IVC, FVC, FEV_1/FVC ratio).

Furthermore, the testosterone and DHEA-S levels were determined by automated ELISA with Emmulite instrument. Statistical processing of the data was done using Microsoft Excel spreadsheets, STATISTICA v6.0 software package and SPSS software package. The quantitative data (with normal distribution) is presented as M ± SD, where M = cohort mean and SD = standard deviation. For correlation analysis of evaluated parameters, the Pearson parametric method and Spearman non-parametric method, were used.

RESULTS

In order to evaluate the influence of hormonal disturbances on the course of COPD, 56 women were examined.

The total testosterone level in examined females with moderate COPD was 0.95 ± 0.69 micromol/L, which was 2 times lower than that of the control group of healthy women of reproductive age (1.9 ± 0.5 nmol/L, p<0.05). Hypoandrogenic state (by total testosterone level) was diagnosed in 22 female patients with moderate COPD and in 41 patients with severe COPD. The increased total testosterone level (more than 2.5 nmol/L) was determined in 2 (4.2 %) female patients with moderate COPD and in 1 severe COPD, with the average of 3.04 ± 0.61 nmol/L. In about 2/3 of menopausal patients (61.9 %) the testosterone concentrations were very low (less than 1 nmol/L). By the hypoandrogenic state in COPD patients we mean the decreased production of not only ovarian but adrenal androgens as well.The DHEA-S concentration (4.79 ± 3.15 micromol/L) in COPD patients was also significantly lower than in healthy women group (8.3 ± 2.1 micromol/L), but remained in normal range.The concentrations of DHEA-S lower than 1.5 micromol/L were observed in 12 % of women with moderate COPD and in 16.7 % women with severe COPD.

The analysis of correlations between clinical parameters and hormonal levels showed revealed the direct correlation between the following parameters: ACT level and the DHEA-S concentration; r=0.73, p< 0.001.between testosterone level and FEV1, r=0.48 with p < 0.001, between FEV1 and DHEA-S level – r=0.861 with p<0.001; between PEF and DHEA-S level – r=0.767. The negative correlation was noted between the duration of the disease and DHEA-S level: r= -0.948, p<0.001. between the number of night time symptoms and testosterone level: r=0.56, p<0.001. Moreover, the following parameters of correlation between respiration rate (RR) and testosterone level were determined: r= -0.4, p<0.05; and between RR and DHEA-S: r= -0.37, p<0.05.

The correlation analysis revealed multiple linear correlations between clinical parameters and hormonal levels.

Thus, the obtained data suggest that the various hormonal disturbances are prevalent and contribute into worsening the clinical course of COPD in women of various ages. Cortisol, the most precise marker of adrenal cortex condition, plays significant role in determining the clinical course of the disease. Furthermore, the comparative analysis of COPD patients in comparison with the group of healthy people had revealed the significant differences in androgen status in females. and also the reverse correlation between the level of hormones and the age and disease duration. The data obtained provide evidence for greater lowering of androgen levels especially in women by mostly lowering DHEA-S levels.

The lowered levels of main adrenal cortex hormones has high prevalence in women with moderate and severe chronic obstructive pulmonary disease. In examination of hormonal status the particular attention should be paid to determination of cortisol, aldosterone as well as of testosterone and DHEA-S.

DISCUSSIONS

The various changes in hormonal profile are often observed in COPD patients and may have effect on the control of the disease and the treatment results. In COPD, the hormone-production insufficiency of the adrenal cortex is most frequently found. The adrenal cortex produces three main types of hormones with multifaceted metabolic effects. The main hormones are cortisol, DHEA and aldosterone. The impaired endocrine functions may worsen the clinical symptoms of COPD, therefore the measures aimed at controlling the disease must include the systematic and appropriate evaluation of endocrine disturbances in COPD patients.

CONCLUSIONS

The deficit of DHEA-S and testosterone is determined in female patients with COPD, and all clinical parameters defining the course of COPD show dependence on all hormonal levels, mostly on DHEA-S. The deficit of hormones worsens the clinical course of chronic obstructive pulmonary disease and asthma control.

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