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AGE-RELATED ANDROGEN DEFICIENCY IN MEN AND A CARDIOVASCULAR DISEASE

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Objective. The purpose of this study is to explore the prevalence of LOH with concomitant cardiovascular disease, and the development of clinical and laboratory-biochemical criteria for the diagnosis of reduced male gonadal function in this group of patients.

Methods and results. The study included 314 patients with cardiovascular disease. Testosterone levels in different clinical situations were as follows: it was noticed that in the absence of sexual complains in patients, normal values of fractional testosterone were observed in 18.2% of cases, marginal values – in 81.8%. The content of the total testosterone in the later case was 2.33+0.2 ng/ml, free testosterone 4.0+0.5 pg/ml. In the presence of complaints of sexual nature, normal testosterone levels were noted in 9.1% of patients, marginal levels in 18.2%, reduced serum testosterone – in 72.7%. In marginal hormonal levels, the average values were as follows: total testosterone - 2.35+0.1 ng/ml, free testosterone 67.9+4.5 pg/ml, in decreased levels: total testosterone – 2.28+0.2 ng/ml, free testosterone -64.1+4.1 pg/ml. Conclusions. Biochemical characteristics of LOH in the presence of a cardiovascular disease is the average level of the total testosterone within the range 2.28 - 2.29 ng/ml, free testosterone – 60.1 - 68.1 pg/ml.

Key words: androgen deficiency, cardiovascular disease.

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INTRODUCTION

In recent years, much attention has been paid to the reproductive health of men in all age groups. This is due to many factors of which increase in the male infertility is an example very much noticed in the general population, particularly in people with endocrine disorders, disorders that lead to a change in the behavior and the development of associated somatic and neuro-psychiatric diseases (Swerdloff & Wang 1993). Another important aspect is the

immense influence of somatic diseases on the male reproductive system, not ruling out the high prevalence of harmful habits such as smoking, high alcohol consumption and many forms of psychoactive substance addiction that adversely affect the secretory function and homeostasis of male sex hormones (Mills et al.1998). The actual very important question is the prevalence, early diagnosis and treatment of the late-onset hypogonadism (LOH) that occurs with the most common group of cardiovascular diseases (Bhasin S et al. 1992).The purpose of this study is to explore the prevalence of LOH with concomitant cardiovascular disease, and the development of clinical and laboratory-biochemical criteria for the diagnosis of reduced male gonadal function in this group of patients.

MATERIALS AND METHODS

The study included 314 patients, 248 (79.0%) of them had no problems of sexual nature and were patients of general practitioners who voluntarily completed the AMS-questionnaire; the remaining patients in this study - 66 men (21%) visited the sexologist with sexual dysfunction complaints; patients also had cardiac dysfunction which included: arterial hypertension (stage 1 to 3) and high risk of complications (59 individuals), obesity (stage 1 to 2) (41 patients), compensated diabetes mellitus (32 patients), pro-atherogenic dyslipoproteinemia (54 patients), metabolic syndrome (62 individuals); erectile dysfunction (66 cases). Patients aged from 40 to 70 years were grouped as follows: 40 to 45 years - 28 patients (8.9%), 46 to 50 years - 35 patients (11.2%), 51 to 55 years - 41 patients (13.1%), 56 to 60 years – 37 patients (11.8%), 61 to 65 - 43 patients (13.7%), 66 to 70 years - 47 patients (14.9%) (Table 1). The clinical diagnosis of LOH is based on the "aging male questionnaire", or the AMS-questionnaire. It conceded the following items: patient's general condition; joint and muscle pain, sweating, insomnia, drowsiness, fatigue, irritability, restlessness, panic attacks, impatience; muscle weakness, depression, feeling of "worthlessness", feeling of emptiness, poor growth of facial hair, decreased libido, decrease in the intensity and quality of erection, decrease in the performance and number of sexual encounters. Results (interpretation of points): from 0 - complete absence of symptoms, up to 5 (very symptomatic). Laboratory diagnosis of LOH was performed using the ELISA method test systems, with the help of a photometer «Multiskan Plus» at a wavelength of levels of the total and free testosterone were determined, these were ranked in three categories - normal, marginal and pathological decrease (Table 2). For statistical processing of the study results, the method for assessment of the significance of differences between two sets by applying the criterion of t-Student was used.

The difference in indicators is true when $t \geq 2$, in this case $p < 0.05$. Student's t criterion was used to identify the main differences between the quantitative characteristics of the study process. During statistical calculations of data, values were put into tables using <<Excel>>, and mathematical and statistical processing was carried out using the program «Stat graphics plus for Windows», version 7.0.

Table 1. Age and nosological characteristics of patients involved in this study

Age (years)	Nosology (number of patients)						
	Arterial hi-pertension	Obesity	Diabetes	Dyslipidemia	Erectile dysfunction	Metabolic syndrome	Total
40 – 45	3	5	3	2	8	7	28
46 – 50	6	6	5	5	7	6	35
51 – 55	9	3	4	8	9	8	41
56 – 60	8	4	5	7	7	6	37
61 – 65	9	4	3	9	9	9	43
66 – 70	24	19	12	23	26	26	130

Table 2. Ranking of the total and free testosterone levels depending on the reduction degree in the blood serum

The degree of reduction of fractional testosterone	Total testosterone (ng/ml)	Free testosterone (ng/ml)
Normal contents	>3.46	>72.00
Marginal decrease	2.31 – 3.46	65.00 – 72.00
Pathological decrease	<2.31	<65.00

Table 3. Testosterone levels in men with metabolic syndrome and sexual dysfunction

Character of the decline in testosterone levels	Number of patients	Level of the total testosterone, ng/ml	Level of free testosterone , ng/ml
Normal level	1 (9.1%)	3.90±0.1	75.9±5.1
Marginal level	2 (18.2%)	2.35±0.1	67.9±4.5
Reduced level	8 (72.7%)	2.28±0.2	64.1±4.1

RESULTS

According to the survey that used a special scale, LOH was detected in 80.7% of cases. The distribution of patients with LOH was of uniform nature up to 60 years: 40 to 50 years – 42.0%, 51 to 60 years – 50.0%, 61 to 70 years – 8.0%. Clinical symptoms of LOH were of the following character: "decline in the general state" 3.3±0.01 points, "increase in the exhaustion" - 2.8±0.01 points, "muscular weakness" - 2.9±0.02 points; "depression" – 2.8±0.02 points, the sense of "everything in the life is already in the past" - 2.6±0.01 points, feeling of "emptiness" - 2.8±0.01 points, "reduced hair growth" – 2.7±0.02 points, reduction in the frequency of sexual intercourse - 2.9±0.02 points, decrease in the morning erection – 2.8± 0.02 points, decreased libido - 2.8±0.01 points, $p<0.05$. Testosterone levels in different clinical situations were as follows: it was noticed that in the absence of sexual complains in patients, normal values of fractional testosterone were observed in 18.2% of cases, marginal values – in 81.8%. The content of the total testosterone in the later case was 2.33±0.2 ng/ml, free testosterone 4.0±0.5 pg/ml. In the presence of complaints of sexual nature, normal testosterone levels were noted in 9.1% of patients, marginal levels in 18.2%, reduced serum testosterone – in 72.7%. In marginal hormonal levels, the average values were as follows: total testosterone - 2.35±0.1 ng/ml, free testosterone 67.9±4.5 pg/ml, in decreased levels: total testosterone – 2.28±0.2 ng/ml, free testosterone -64.1±4.1 pg/ml (Table 3).

DISCUSSION

In recent years, considerable attention has been paid to the polymorbidity and the widespread aggravation of diseases. We are analysing the issue of progression, diagnosis and treatment of diseases in individuals aged 50 years and over from these aspects. There is no exception to LOH, which often develops as a result of concomitant somatic and neuropsychiatric diseases. Effects of somatic and psycho-neurological pathology in LOH can significantly reduce both the quality of disease diagnosis and the effectiveness of prevention, likewise, the treatment programmes.

It should be noted that, in general, LOH develops in persons over 50 years, and there is an accumulation of a number of age-related and pathological changes at this age that contribute to the alteration of the disease progress (Rolf et al. 2002).These features include:

1. There is an overall increase in pathological conditions, when there is a corresponding increasing number of nosological forms, dominated by chronic diseases, characteristic of polymorbidity (Schill 2001).

2. Peculiar etiological characteristics in

diseases of the elderly are affected by internal environmental factors (age-related changes in organ systems, metabolism and regulation) that increase the aggressiveness of pathogens and lower resistance of the elderly (Boyanov et al 2003).

3. Peculiarity of the pathological pathogenesis in the middle and old age quite often changes the specific pathogenic mechanisms of disease (Tenover 1992).

4. Clinical characteristics of diseases in the elderly: diseases usually are atypical – less symptomatic, latent, diseases mask themselves as other diseases, and are often very severe, more often disabling, more likely to relapse, and often the transition of acute forms to chronic ones take place, shorter latent period of the disease; leading to frequent complications, reduced time to the development of complications, by increasing the functional decompensation of the affected system, thus the reduction of the life expectancy of the patient (Bonithon-Kopp et al. 1988). Thus, patients above 50 year of age with a cardiovascular disease are prone to the development of LOH. On the other hand, testosterone deficiency can also result in the development of a vicious circle within the cardiovascular diseases cycle. Therefore, the influence of androgens on the cardiovascular system is very significant. It has been established that there is a direct effect of androgens on the vascular wall, and this results in the modulation of the activity in the potassium channels and stimulation of the secretion of nitric oxide. This results in a vasodilating effect. The positive effect of testosterone mainly undertaken by estrogen, because it is the major source of estrogen. Estrogens have direct protective effects on cardiomyocytes. Age-related reduction of the testosterone concentration, on its turn, reduces estrogen levels, that, on its turn, leads to the overall reduction of the efficiency of cardioprotection (Kula, Slowikowska-Hilczer 2000). Androgens have a positive effect on the hemostatic system. This is reflected in its ability to reduce the level of fibrinogen, proconvertin clotting factor VII. At the same time, a number of studies have shown that testosterone seems to have pro-aggregation properties due to its ability to lower the activity of cyclooxygenase and to reduce anti-aggregatory effects of prostaglandins. Testosterone, as shown in several studies, has anti-atherogenic effects, particularly, a low level of testosterone is associated with a high degree of occlusion of the coronary artery. This is the pathogenic relationship between a cardiovascular disease and LOH. This was confirmed in our studies, and applied in the practice by the development of LOH diagnostics algorithms in the most common disease of the heart and blood vessels (Mitchell et al. 1995).

CONCLUSION

The study showed that a cardiovascular disease-related LOH occurs from the age of 40 – 50 years. LOH in association with cardiovascular diseases is characterized by such symptoms like general weakness, difficulty in falling asleep and a daytime sleepiness, irritability, panic attacks, development of a sense of "lifelessness", as well as decreased libido, decrease in morning erections, decrease in the frequency of sexual activities. Biochemical characteristics of LOH in the presence of a cardiovascular disease is the average level of the total testosterone within the range 2.28 - 2.29 ng/ml, free testosterone – 60.1 - 68.1 pg/ml.

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