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LATE – ONSET HYPOGONADISM AND ARTERIAL HYPERTENSION

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Arterial hypertension is characterized by development of late-onset hypogonadism and clinically relevant decrease of total and free testosterone levels in older male patients.

To investigate signs and symptoms of late-onset hypogonadism, a health assessment questionnaire was used in two patient groups; also serum bound and free testosterone levels were measured by immunofluorescence method. Results: Fall of total and free serum testosterone levels below the level of late-onset hypogonadism diagnostic criteria was observed in male patients over 40 years of age with arterial hypertension. In males of similar age group and free of arterial hypertension there was normal testosterone level or a borderline decrease of serum testosterone level and no clinical presentations of hypogonadism. Conclusions: The study data prove the importance of the diagnosis of late-onset hypogonadism in adult male over 40 years of age with arterial hypertension.

Key words: arterial hypertension, late-onset hypogonadism.

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INTRODUCTION

Arterial hypertension is a common disease in the general population, and it has different socially significant complications: myocardial infarction, stroke, chronic heart failure. In addition, arterial hypertension may be associated with poorly studied symptoms, such as male late-onset hypogonadism (LOH) (Swerdloff & Wang 1992). LOH is an age-related clinical and biochemical syndrome, which is characterized by typical symptoms and reduced level of serum testosterone. Neurovisceral, psychological and sexual disorders underlie the development of hypogonadism, impairing the quality of life (Isidori et al. 2005). Data on the correlation of the testosterone deficiency with the development of the cardiovascular diseases are available. Testosterone affects vasoconstriction and vasodilatation, as well as the synthesis of and nitric oxide (NO). Generally, there are data showing that testosterone reduces the endothelial dysfunction and aids to decrease vasospasm of coronary blood vessels, rupture of atherosclerotic plaque, and thrombosis (Manolakou et al. 2009). Various research studies show negative correlation between the level of endogenous androgen and the development of atherosclerosis (Heinemann et al. 1999).

Table 1. Baseline characteristics of the study population

Parameter	Patients with arterial hypertension who underwent antihypertensive treatment, (n=320)	Normotensive patients (n=402)
Average age, years	56.2 ± 0.7	54.1 ± 0.8
Hypertrophy of left ventricle, %	98.0	11.4
Cholesterol, mmol/L	4.9 ± 1.3	4.9 ± 1.6
HHigh-density lipoprotein, mmol/L	1.12 ± 0.5	1.14 ± 0.4
Triglycerides, mmol/L	1.4 ± 0.2	1.5 ± 0.1
Glucose, mmol/L	4.9 ± 0.4	5.0 ± 0.3
Systolic blood pressure, mm Hg	149.8 ± 1.2	120.1 ± 0.9
Diastolic blood pressure, mm Hg	96.6 ± 1.5	86.4 ± 0.9

[1] Metabolic parameters determined on the background of appropriate therapy, blood pressure values measured on the background of appropriate antihypertensive therapy.

Table 2. Levels of testosterone in male patients with arterial hypertension and in normotensive males

Parameter	Patients with arterial hypertension who underwent antihypertensive treatment (n=320)			Normotensive patients (n=402)		
	40-49 (n=102)	50-59 (n=86)	> 59 years (n=132)	40-49 (n=99)	50-59 (n=103)	> 59 years (n=200)
Total testosterone level, ng/ml	2.46±0.2*	2.45±0.1*	2.09±0.3*	3.56±0.3*	3.49±0.1*	3.14±0.1*
Free testosterone level, pg/ml	58.23±3.5*	59.21±3.*	54.01±2.4*	73.34±3.0*	74.15±2.7*	70.05±1.8*

* $p<0.05$

Data on correlation and reciprocal influence of hypogonadism and arterial hypertension are available in the literature (Boyanov et al. 2003)8). The goal of our study is comparing the testosterone levels in males over 40 years of age suffering from arterial hypertension and the testosterone levels in normotensive males in the same age group

MARTERIAL AND METHODS

An open prospective study was conducted in two groups of men. The first group included 320 patients with diagnosed arterial hypertension who underwent antihypertensive treatment (1 or 2 medical products). The second group involved 402 patients with no physical pathologies, including arterial hypertension, found during clinical assessment. The patients from the both groups were divided into three age subgroups: 40-49 years old, 50-59 years old, 60 years old and older.

Patient inclusion criteria. Stage 1-2 arterial hypertension and high risk of cardiovascular complications for the study group.

Table 3. Results of health assessment questionnaire in hypogonadal men with arterial hypertension and normotensive male patients

Item of questionnaire	Score	
	Hypogonadal male patients with arterial hypertension (n=320)	**Normotensive patients with borderline testosterone level (n=402)**
General performance	1.1±0.01*	2.5±0.02*
Joint and muscle pain accompanied by low back pain	2.4±0.01*	1.1±0.02*
Hydropoiesis accompanied by occasional sweating	3.2±0.01*	1.05±0.03*
Insomnia	3.3±0.02*	1.4±0.01*
Somnolence, fatigue	2.1±0.002*	1.3±0.02*
Irritability	4.2±0.004*	1.4±0.03*
Restlessness, hypersensitivity	2.2±0.002	1.3±0.001*
Panic attacks	3.6±0.01*	1.5±0.02*
Exhaustion signs	2.1±0.001*	1.4±0.003*
Muscle weakness	2.1±0.002	1.2±0.002*
Depression signs	3.3±0.01*	1.2±0.02*
Feeling that "everything has gone"	2.2±0.01*	1.4±0.02*
Aching void	2.1±0.002*	1.9±0.001*
Decrease of facial hair growth	3.3±0.02*	1.2±0.01*
Decrease of sexual satisfaction and frequency of sexual acts	3.4±0.02*	1.6±0.01*
Decrease of number and intensity of morning erection	3.4±0.01*	1.4±0.02*
Decreased libido	3.5±0.02*	1.3±0.01*

* $p<0.05$

Patient exclusion criteria. Decompensated diseases, oncological pathology, diseases characterized by significant cognitive deterioration and impeding contact with patient, history of stroke or myocardial infarction, other stages of hypertension, or risk of cardiovascular complications of hypertension.

Confirmation of diagnosis. Diagnosis of arterial hypertension was confirmed according to the WHO recommendations. For the diagnostics of the symptoms of late-onset hypogonadism in the both patient groups, an Aging Males' Symptom Questionnaire recommended for the use in the clinical practice by the International Society for the Study of the Aging Male (see Table 3). The patients have evaluated their symptoms and indicated the total score that corresponded to the extent of the symptoms, where "1" represented for the absence of a symptom, and "5" – a very significant symptom. If the total score did not exceed 26, the symptoms and signs of LOH was evaluated as "insignificant"; if the total score was 27-36, the symptoms and signs of LOH was evaluated as "of minor significance"; at the total score of 37- 49 – as "of medium significance"; whereas, at the total score of 50 – as "very significant"(Wang et al. 2009).

Total and free testosterone serum levels were measured by immunofluorescence method with "Immulite 2000" analyser, manufactured by Siemens Healthcare Diagnostics, method identification – TESTOSG. The results of the health assessment questionnaire and measurements of free and total serum testosterone levels were compared between the study group and the control group by nonparametric statistics. Total testosterone levels exceeding 3.46 ng/ml were considered normal, the norm for free testosterone levels was set at 72.0 pg/ml (Wang et al. 2009). Statistical data processing was performed using the SPSS (Statistical Package for the Social Sciences) 20.0 software.

RESULTS

See Table 1 for baseline characterization of study population**.** In male with hypertension aged 40-49 years, 50-59 years and over 60 years of age, the total and free testosterone serum levels were below the level of late-onset hypogonadism diagnostic criterion. The levels were significantly lower in comparison to healthy patients aged 40-49 and 50-59 years, whose total and free testosterone levels were within the age limits, but the testosterone levels in healthy males over 60 years of age has decreased to the borderline level, $p<0.05$ (Table 2). In comparison to healthy male patients of similar age group, the sexual symptoms, physical and psychological state subscores of clinical presentation in hypogonadal male patients over 40 years of age were decreased accordingly (Table 3).

DISCUSION

At present arterial hypertension is considered to be a general pathology characterized by a complex of neurohormonal changes and polypathogenic effects, notable hypertrophy of resistance vessels, endothelial dysfunction, ion membrane homeostasis disorder, water retention etc (Boyanov et al. 2003, Kula & Slowikowska-Hilczer 2000, Mills et al. 1998). These changes increase the risk of cardiovascular complications of hypertension. Recently, a considerable number of publications confirming the relation of decreased testosterone level to cardiovascular complications in arterial hypertension have been published (Isidori et al. 2005). It has been found that age-dependent decrease of serum testosterone levels is associated not only with the risk of sudden cardiovascular death, but also with the risk of cerebral and cardiac disorders (Schill 2001, Tenover 1999, Mitchell et al. 1995). The comparison of different age groups has allowed to demonstrate that total and free serum testosterone levels are low in hypertensive male patients over 40 years of age, and that the levels of total and free testosterone in healthy patients is normal or reach borderline values. In hypertensive patients in this age group, psychological and sexual LOH symptoms are more significant.

CONCLUSIONS

Arterial hypertension in older male patients is characterized by development of late-onset hypogonadism and clinically relevant decrease of total and free testosterone levels. In healthy male patients of similar age group, there is normal testosterone serum level or a borderline decrease of testosterone serum levels without clinical presentations of hypogonadism. The study data prove the importance of the diagnosing the late-onset hypogonadism in male patients over 40 years of age with arterial hypertension.

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