CLINICAL AND EPIDEMIOLOGICAL CHARACTERISTICS OF MALE HYPOGONADISM IN TYPE 2 DIABETES IN RUSSIA: COMBINED ANALYSIS OF STUDY DATA FOR THE PERIOD 2005–2022

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BACKGROUND: Male hypogonadism is associated with type 2 diabetes mellitus (T2DM), therefore, it is of interest to study its clinical and epidemiological characteristics. These data are published, but their fragmentation and small sample sizes are a problem. A summary assessment of the combined primary data of the conducted studies will provide sufficient representativeness and will allow to extrapolate the results to the general Russian population with T2DM.
AIM: Assessment of the clinical and epidemiological characteristics and aggravating factors of male hypogonadism in T2DM in Russia.
MATERIALS AND METHODS: A Combining primary data (anamnesis, anthropometric indicators, laboratory tests) of full-design, cross-sectional, screening studies of hypogonadism in men with T2DM conducted on the territory of the Russian Federation in the period from 2005 to 2022. The groups were compared using the Mann-Whitney U-test for quantitative indicators and χ^2 with Yates' correction for qualitative ones. Differences were considered statistically significant with p <0,05. The groups were compared using the Mann-Whitney U-test and χ^2 with Yates correction. Differences were considered statistically significant at p<0.05.
RESULTS: Hypogonadism was detected in 893 of 1576 men (56,7%) with T2DM. Patients with hypogonadism were statistically significantly older, had higher body mass index (BMI), worse glycemic control than eugonadal men. There was statistically significantly higher prevalence of macroangiopathies and polyneuropathy in hypogonadal patients.
CONCLUSION: The prevalence of male hypogonadism in T2DM 56,7%. Its development is due to age, obesity, worse glycemic control. Hypogonadism syndrome is associated with the development of diabetic macroangiopathy and polyneuropathy. Severe violation of glycemic control (glycated hemoglobin (HbA_{1c}) 10% or more) significantly reduces testosterone production and increases the prevalence of hypogonadism.

KEYWORDS: testosterone; men; hypogonadism syndrome; diabetes mellitus

КЛИНИКО-ЭПИДЕМИОЛОГИЧЕСКИЕ ХАРАКТЕРИСТИКИ СИНДРОМА ГИПОГОНАДИЗМА У МУЖЧИН С САХАРНЫМ ДИАБЕТОМ 2 ТИПА В РОССИЙСКОЙ ФЕДЕРАЦИИ: ОБЪЕДИНЕННЫЙ АНАЛИЗ ДАННЫХ ИССЛЕДОВАНИЙ ЗА ПЕРИОД 2005–2022 ГГ.

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ОБОСНОВАНИЕ. Мужской гипогонадизм ассоциирован с сахарным диабетом 2 типа (СД2), в связи с этим представляет интерес исследование его клинико-эпидемиологических характеристик. Эти данные опубликованы, однако проблемами являются их разрозненность и малые объемы выборок. Суммарная оценка объединенных первичных данных проведенных исследований обеспечит достаточную репрезентативность и позволит экстраполировать результаты на российскую популяцию пациентов с СД2 в целом.
ЦЕЛЬ. Оценка клинико-эпидемиологических характеристик и отягощающих факторов синдрома гипогонадизма у мужчин с СД2 в России.
МАТЕРИАЛЫ И МЕТОДЫ. Объединение первичных данных (анамнеза, антропометрических показателей, лабораторного исследования) сплошных одномоментных скрининговых исследований синдрома гипогонадизма у мужчин с СД2, проведенных на территории Российской Федерации в период с 2005 по 2022 гг. Сравнение групп проведено с помощью U-критерия Манна–Уитни и χ^2 с поправкой Йейтса. Статистически значимыми считались различия при p<0,05.
РЕЗУЛЬТАТЫ. Синдром гипогонадизма был выявлен у 893 (56,7%) из 1576 мужчин. Пациенты с гипогонадизмом были статистически значимо старше, имели худшие показатели гликемического контроля и более выраженное ожирение по сравнению с мужчинами без гипогонадизма. При оценке характера осложнений СД2 была выявлена статистически значимо большая распространенность макроангиопатий и полинейропатии у мужчин с гипогонадизмом.

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ЗАКЛЮЧЕНИЕ. Синдром гипогонадизма был выявлен у 56,7% мужчин с СД2. Его развитие обусловлено возрастом, ожирением, нарушением контроля углеводного обмена. Синдром гипогонадизма ассоциирован с развитием диабетических макроангиопатий и полинейропатии. Выраженное нарушение контроля углеводного обмена (гликированный гемоглобин HbA_{1c} 10% и более) усугубляет снижение выработки тестостерона и повышает распространенность гипогонадизма.

КЛЮЧЕВЫЕ СЛОВА: тестостерон; мужчины; синдром гипогонадизма; сахарный диабет

BACKGROUND

Male hypogonadism often accompanies type 2 diabetes mellitus (DM2), while these diseases have a mutually aggravating effect [1-3]. It is known that key components of the metabolic syndrome, such as obesity and DM2, suppress the gonadotropic function of the pituitary gland through various mechanisms. This leads to a deficiency in testosterone, which negatively affects fat and carbohydrate metabolism and forms a pathological «vicious circle» [4– 7]. Compared with healthy men, those with DM2 have, on average, a level of total testosterone 2.5 nmol/L lower, and the prevalence of hypogonadism is higher and may be more than 50% according to estimates of both domestic [8–10] and foreign researches [7, 11–13]. According to I.A. Khripun et al. (2021), laboratory-confirmed hypogonadism was detected in 124 (44.9%) of 276 men with DM2 included in the analysis [8]. And in the research of T.Y. Demidova et al. (2022) this index was 50.81% (63 out of 124 patients) [9]. In Russia for the period from 2005 to 2022 a number of single- and multicenter researches have been conducted to study the clinical and epidemiological characteristics and aggravating factors of the male hypogonadism with varying degrees of control and duration of DM2 and varying degrees of overweight [14–18]. However, the data of these researches have never been analyzed integratively, and this reduced the statistical power and representativeness. A summary assessment of the primary data of the conducted researches, performed on samples of patients with different characteristics and volume, will provide sufficient representativeness and will allow extrapolating the results to the general Russian population.

AIM

Assessment of the clinical and epidemiological characteristics and aggravating factors of male hypogonadism in type 2 diabetes.

MATERIALS AND METHODS

Study design

Pooled analysis of data obtained as a result of full-design, cross-sectional, screening single- [15, 17, 18] and multicenter [14, 16] non-interventional studies conducted on the territory of the Russian Federation in the period from 2005 to 2022.

Study sites, start and end dates

Sites. The study included men with DM2 who applied for medical care at the National Medical Research Center for Endocrinology of the Ministry of Health of the Russian Federation, as well as other medical organizations in various regions of the Russian Federation [14–18]. The study organization in regional centers and the processing of the obtained data were carried out under the guidance of the National Medical Research Center for Endocrinology of the Ministry of Health of the Russian Federation.

Study time. Analysis of material collected between 2005 and 2022.

Studied populations

Inclusion criteria: male gender, age 40–65 years, established diagnosis of DM2 in accordance with current recommendations [19].

Exclusion criteria: gender and developmental disorders; the absence of at least one of the testicles, cryptorchidism, injuries and / or surgical interventions on the genitals; taking androgen, anabolic steroids, gonadotropins, antiestrogen or antiandrogen at the time of the research or in history; alcoholism or drug addiction.

Withdrawal criteria: not provided.

Description of medical intervention

For study blood was taken in the morning on an empty stomach from the cubital vein.

Key outcomes

An index of the incidence of male hypogonadism with DM2, as well as its relationship with the compensation of carbohydrate metabolism, complications, and the received hypoglycemic therapy.

Secondary outcomes

Analysis of the aggravating effect of age and obesity on hypogonadism.

Subgroup Analysis

Groups of hypo- and eugonadal patients were compared across the entire sample. Besides, there was performed an additional analysis of the male groups depending on age, glycated hemoglobin (HbA1c), body mass index (BMI) to evaluate the correlation between the frequency of hypogonadism, its severity and age, glycemic control, and the severity of overweight.

Methods

Anamnestic data were obtained through a survey and an analysis of medical records. Physical examination assessed the condition of the genital hair, mammary glands and external genitalia. The level of total testosterone was determined using enzyme-linked immunosorbent assay (ELISA) on a Vitros 3600 Immunodiagnostics System (Johnson and Johnson, USA) using enhanced chemiluminescence in 4 out of 5 researches included in the analysis [14-17], as well as using high-performance liquid chromatography with tandem mass spectrometry (HPLC-MS/MS) on an Agilint 1290 Infinity II chromatograph, AB Sciex TripleQuad 5500 mass spectrometer in the latest study [18]. The reference ranges

were the same in all cases – laboratory confirmation of hypogonadism was the level of total serum testosterone less than 12.1 nmol/L. The level of HbA1c was determined by ion exchange high performance liquid chromatography (HPLC) using an automatic analyzer BIO-RAD D10.

Statistical analysis

Principles of Sample Size Calculation: was not calculated, the analysis included data of all patients meeting the inclusion criteria [14–18].

Methods of statistical analysis: statistical processing of the obtained data was carried out using the analytics software package STATISTICA (StatSoft Inc. USA, version 8.0); quantitative data are presented as medians and boundaries of the interquartile range, qualitative data are presented as percentages; the groups were compared using the nonparametric χ^2 method with the Yates correction for qualitative traits and the Mann–Whitney U test for quantitative traits. Differences were considered statistically significant at $p<0.05$.

Ethical review

The researches included in the pooled analysis were approved at the meetings of the relevant local ethical committees [14–18].

RESULTS

Participants of the pooled research analysis

The analysis included 1576 men with DM2. The general characteristics of the patient sample are presented in Table. 1.

Main results of the research

All men included in the pooled analysis had some non-specific symptoms that could potentially be clinical manifestations of hypogonadism. At the same time, a decrease in the level of total testosterone was revealed in 893 men. Thus, the incidence of hypogonadism was 56.7%.

When comparing groups of hypo- and eugonadal patients, statistically significant differences were revealed in a number of indices (Table 2).

Thus, patients with hypogonadism were statistically significantly older, had worse glycemic control and more severe obesity compared with men who had normal testosterone levels.

The assessment of the incidence of DM2 complications and the analysis of the received hypoglycemic therapy were carried out only in 3 out of 5 considered researches [14, 15, 18], therefore the comparison of patients according to the above indices was carried out separately (Table 3).

When comparing patients with and without hypogonadism, according to the complications and hypoglycemic therapy, a statistically significantly higher prevalence of macroangiopathies (coronary heart disease (CHD), acute cerebrovascular accident (ACV) in history, diabetic foot syndrome (DFS)) and polyneuropathy in group of patients with hypogonadism compared with patients without it. At the same time, there were no significant differences in the incidence of microangopathy (retinopathy and nephropathy), as well as acute myocardial infarction (AMI). Also there were no significant differences in the taken hypoglycemic therapy.

Table 1. General characteristics of the patient sample

Parameter	[14], 2006 (n=335)	[15], 2006 (n=82)	[16], 2019 (n=554)	[17], 2022 (n=100)	[18], 2022 (n=505)	Σ (n=1576)
Age, years	56 [51; 65]	53 [47; 61]	55 [50; 58]	45.5 [43; 48]	58 [52; 62]	55 [50; 60]
HbA1c level, %	7.8 [6.8; 9.4]	6.9 [6.3; 8.7]	7.3 [6.2; 8.9]	8.8 [6.9; 11.6]	8.6 [7.3; 10.2]	7.9 [6.6; 9.6]
Total testosterone level, nmol/L	11.3 [8.2; 15.4]	8.5 [5.7; 11.9]	12.5 [9.1; 16.4]	12.8 [7.8; 15]	10.0 [7.4; 12.9]	11 [7.9; 14.74]
BMI, kg/m^2	29.4 [26.0; 32.4]	29 [25; 31]	30.6 [28.0; 34.3]	27.3 [26.0; 28.7]	31.8 [28.4; 35.9]	30 [27.1; 33.9]
Incidence of hypogonadism, %	50.4	75.6	48.0	41.0	70.3	56.7

Notes: quantitative data are presented in the form of medians and boundaries of the interquartile range, qualitative data are presented in the form of percentages. HbA1c — glycated hemoglobin, BMI — body mass index.

Table 2. Comparison of patients depending on the presence of hypogonadism

Parameter	Hypogonadism (n=893)	No hypogonadism (n=683)	p
Age, years	56 [50; 60]	55 [49; 59]	**<0.001**
HbA1c level, %	8.2 [6.8; 9.9]	7.6[6.4; 9.2]	**<0.001**
Total testosterone level, nmol/L	8.4 [6.7; 10.1]	15.7[13.5; 18.6]	**<0.001**
BMI, kg/m^2	31.0 [27.8; 35.1]	29.4[26.5; 32.6]	**<0.001**

Notes: U is the Mann-Whitney criterion; quantitative data are presented in the form of medians and boundaries of the interquartile segment. HbA1c — glycated hemoglobin, BMI — body mass index.

Table 3. Comparison of patients by the frequency of complications of DM2 and the resulting hypoglycemic therapy, depending on the presence of hypogonadism

Parameter	Hypogonadism (n=586)	No hypogonadism (n=336)	p
Complications of DM2, %			
Retinopathy	42.7	43.5	0.870
Nephropathy	30.4	30.5	0.945
Polyneuropathy	70.4	58.8	**<0.001**
CHD	32.7	23.8	**0.005**
AMI history	11.0	8.7	0.318
CVA history	6.1	0.9	**<0.001**
DFS (all forms)	25.2	14.5	**<0.001**
Hypoglycemic therapy, %			
Non-insulin therapy (diet, OHAs, GLP-1 receptor agonists)	60.0	58.3	0.655
Insulin therapy (+basal, +basal-bolus)	40.0	41.7	0.655

Notes: χ^2 adjusted by Yates; qualitative data are presented as percentages. DM2 — type 2 diabetes mellitus; CHD — coronary heart disease; AMI — acute myocardial infarction; CVA — acute cerebrovascular accident; DFS — diabetic foot syndrome; OHAs — oral hypoglycemic therapy; GLP-1 receptor agonist — glucagon-like peptide-1 receptor agonists.

Additional research findings

Taking into account the statistically significant difference between groups of patients with and without hypogonadism, in age, body weight and adequacy of glycemic control, and a sufficient total sample size, an additional analysis was carried out in subgroups of patients for a more detailed assessment of the age factor, body weight and DM2 control influence on the incidence of hypogonadism and the level of total testosterone.

In the age group of 40–49 years, the incidence of hypogonadism was 49.2%, which was statistically significantly lower than in the age group of 50–59 years — 57.1% (p=0.014), and even more so than in the age group 60–65 years old — 62.0% (p<0.001), while the incidence of hypogonadism in the 60–65 years old group did not statistically significantly differ from that in the 50–59 years old group (p=0.112). Thus, the prevalence of hypogonadism increases with age, which is more pronounced in the relatively young age group. As for the level of total testosterone, it was in the age groups: 40–49 years — 11.6 [8.1; 15.1] nmol/L, 50–59 years — 11.0 [7.9; 14.7] nmol/L, 60–65 years — 11.0 [7.9; 14.2] nmol/L. There were no statistically significant differences in this indices (p>0.05 for all pairs of comparisons).

The influence of the severity of obesity was more notable. Thus, the incidence of hypogonadism in men with a BMI of 29.9 kg/м^2 and less was 49.3%, which is statistically significantly lower than in the group of men with a BMI of 30.0–39.9 kg/m^2 — 60.7% (p<0.001), and even more so in comparison with patients with a BMI of 40.0 kg/m^2 or more — 76.5% (p<0.001). The incidence of hypogonadism in the groups of men with a BMI of 30.0-39.9 kg/m^2 and 40.0 kg/m^2 and more also differed statistically significantly (p=0.003). The levels of total testosterone in individuals with a BMI of 29.9 kg/m^2 or less were 12.2 [8.7; 16.0] nmol/L and statistically significantly differed from those in men with a BMI of 30.0–39.9 kg/m^2 — 10.6 [7.8; 14] nmol/L (p<0.001) and BMI of 40.0 kg/m^2 or more — 8.4 [6.4; 11.0] nmol/L (p<0.001). The levels of total testosterone in the groups of men with a BMI of 30.0–39.9 kg/m^2 and 40.0 kg/m^2 and more also differed statistically significantly (p<0.001). Thus, as body weight increases, both the incidence of hypogonadism increases and total testosterone levels decrease.

In addition, statistically significant differences were obtained in the incidence of hypogonadism in men with an HbA1c level <6.5 — 44.8% compared with men with an HbA1c level of 6.5–7.9 — 57.2% (p<0.001), with the HbA1c group 8.0–9.9 — 57.7% and the HbA1c group ≥10.0% — 66.6% (p<0.001). At the same time, the incidence of hypogonadism did not statistically significantly differ in patients in the HbA1c group of 6.5–7.9% compared to the HbA1c group of 8.0–9.9% (p=1.0), but differed in comparison with the HbA1c group. ≥10.0% (p=0.011). The incidence of hypogonadism in the HbA1c groups 8.0–9.9% and ≥10.0% also differed significantly (p=0.016). As for the testosterone level, men with an HbA1c level <6.5% had this indices 12.5 [8.3; 15.6] nmol/L and it did not differ statistically significantly from that observed in patients in the HbA1c 6.5–7.9% group — 11.0 [8.1; 15.0] nmol/L (p=0.08), however, it was statistically significantly higher than in groups with HbA1c 8.0–9.9% – 11.0 [8.0; 14.4] nmol/L (p=0.013) and HbA1c ≥10.0% — 9.7 [7.2; 13.3] (p<0.001). Also, the levels of total testosterone were not statistically significantly different in the HbA1c 6.5–7.9% and HbA1c 8.0–9.9% groups (p=0.474), but differed in comparison with the HbA1c group ≥10.0% (p= 0.002). Testosterone levels in the HbA1c 8.0–9.9% and ≥10.0% groups were statistically significantly different (p=0.011).

Adverse events

Not noted.

DISCUSSION

Summary of the main result of the research

56.7% of men with DM2 had hypogonadism. Development of hypogonadism is associated with obesity and unsatisfactory glycemic control, as well as the additional influence of the age factor.

Discussion of the main result of the research

A high incidence of hypogonadism in men with DM2 is demonstrated in foreign and domestic researches. Also a well-known fact is the pronounced variability of this indicator, i.e. from 15 to 80% according to various data [7, 9, 11, 13, 20]. This is probably due to a number of factors: the age of patients, the presence and severity of obesity, the degree of DM2 control [4, 21, 22]. Thus, in one of the domestic researches of 2005 included in our analysis with a sample of 82 middle age inpatients with multiple complications of DM2 and concomitant diseases, the incidence of testosterone deficiency was 68–83%, depending on the method of its detection (68.3% when determining total testosterone by ELISA and 83% when calculating its free fraction, respectively) [15]. The discrepancy between the indices of total and free testosterone is associated with an age-related increase in the level of sex hormone-binding globulin (SHBG), leading to an accelerated drop in the concentration of free testosterone against the background of its general decrease [4]. In our analysis, free testosterone was not assessed due to the small amount of primary data on the above index. Our data are comparable with the results of a recent single-center research in 2022, conducted on a sample of 505 also inpatient comorbid patients with the determination of total testosterone by HPLC-MS/MS, in which the incidence of hypogonadism was 70.3% [18]. At the same time, in a multicenter domestic research in 2019 among 554 men with DM2, the prevalence of hypogonadism was only 32.7% [16]. It is worth noting that the sample was characterized by good glycemic control. A summary analysis of the primary data of 5 domestic researches conducted over 18 years among inpatients and outpatients in various medical centers in Russia showed the prevalence of hypogonadism among men with DM2 in the Russian population 56.7%.

The prevalence of hypogonadism increases with age. Our results are comparable with the data of most foreign researchers [22–26]. Thus, the average level of total testosterone in plasma does not change significantly until the age of 50–55 years, and then decreases at a rate of about 1% per year [26], while free testosterone begins to decline from about 35 years of age [27–28]. However, the Massachusetts Male Aging Study shows slightly different numbers: a decrease in the secretion of total testosterone occurs by 2.8% per year (according to earlier data, by 0.4% per year), and free — by 2.5% per year (according to earlier data, by 1.2% per year) [23,24].

The pathogenesis of age-related testosterone production decrease is based on a number of processes. So, older men has a changes in the secretion of luteinizing hormone (LH): the frequency of hormone release's peaks increases and their amplitude decreases, which, according to some scientists, may lead to a decrease in the sensitivity of Leydig cells to the stimulating effect of LH [29]. In addition, the same researches demonstrate a violation of the testosterone's pulse secretion while maintaining the basal. At the same time, exogenous administration of gonadotropin-releasing hormone (GnRH) leads to the restoration of the LH secretion rhythm, which clearly demonstrates the primary disorder at the level of the hypothalamus and the role of its dysfunction in the pathogenesis of age-related androgen deficiency [30]. At the same time, long-term GnRH infusions in this group of patients do not lead to a complete restoration of testicular testosterone production, which is probably associated with a parallel developing damage at the level of Leydig cells, which progresses with increasing age of patients [30–32].

In addition, do not forget about the above-mentioned age-related increase in SHBG synthesis by the liver and the inhibitory effect of testosterone itself on SHBG production.

Thus, two key pathogenetic mechanisms can be identified at the basis of the age-related decrease in testosterone: a decrease in the secretion of testosterone in the testicles (decrease in the stimulating effect of LH and dysfunction of Leydig cells) and an increase in the concentration of SHBG.

The timing of the onset of age-related male hypogonadism is significantly affected by severe somatic diseases, which shift the physiological timing of the onset of a decrease in androgen secretion by an average 5–7 years. Among chronic diseases that accelerate the development of age-related androgen deficiency, obesity and DM2 are of primary importance [4].

In our work, we revealed a dependence of the incidence of hypogonadism and a decrease in total testosterone levels on the severity of obesity. This dependence has been demonstrated in various researches and is due to a functional impairment of negative feedback in the hypothalamus-pituitary-testis system [6, 7, 33–35]. This condition is based on a number of mechanisms. It is known the aromatase of excess adipose tissue in increased amounts converts androgens (testosterone and androstenedione) into estrogens [36, 37]. Estrogens suppress (in amplitude and frequency) the secretion of both GnRH and LH, which manifests as a decrease in the level testosterone in the blood, i.e. secondary hypogonadism, mainly normogonadotropic and potentially reversible with the elimination of obesity [34]. In addition, inadequately low secretion of gonadotropins was previously established with exogenous administration of GnRH to men with DM2 and obesity [38]. It was also shown that hypogonadism can develop due to the resistance of the central hypothalamic-pituitary structures to leptin in obesity and impaired secretion of GnRH and gonadotropins against this background [39]. Functional suppression of regulatory hormones under the influence of the above factors leads to a decrease in their stimulating effect on steroidogenesis in Leydig cells.

The analysis of researches of the Russian population showed that poor glycemic control is associated with a decrease in testosterone levels, which is consistent with a number of foreign publications [35, 40]. The pathogenesis of the mutual influence of hyperglycemia and the production of testosterone by Leydig cells is probably based on a number of mechanisms. Thus, recent researches have shown that hyperglycemia-mediated activation of Toll-like receptor 4 (TLR4) in testicular cells, especially in Leydig cells, can cause oxidative stress and inflammation, which, in turn, leads to testicular dysfunction [41, 42]. Earlier researches, including animal models, also demonstrate an increase in the concentration of pro-oxidants and a decrease in the concentration of antioxidants in DM [43, 44].

Testosterone probably has a dual effect on carbohydrate metabolism:

1. Increases tissue sensitivity to insulin by directly affecting gene expression of insulin receptor B-subtype (IR-β), insulin receptor substrate 1 (IRS-1), protein kinase B (Akt-2), glucose transporter type 4 (GLUT4) [5, 45];
2. Increases insulin secretion stimulated by glucose due to direct action on the androgen receptor in β-cells, which potentiates the insulinotropic action of glucagon-like peptide-1 [46].

At the same time, there are no researches in the literature demonstrating the level of HbA1c, in which it is first necessary to start correcting carbohydrate metabolism and only when the target level of this index is reached, to evaluate and correct the androgenic status of a man, if necessary [47]. Due to this, it is of interest to identify this level. According to our analysis and a recent research [17], an unambiguous negative effect on the incidence of hypogonadism and its severity is exerted by an HbA1c level more than 9.9%, which requires a primary correction of carbohydrate metabolism with an assessment of sex hormones in dynamics. Significant influence on the levels of total testosterone is exerted only by a pronounced decompensation of carbohydrate metabolism, characterized by an increase in the level of HbA1c to 10.0% or more. For patients with HbA1c in the range of 6.5–9.9%, there is no exact evidence of associations between HbA1c levels and testosterone production. According to our data, the main influence on the production of testosterone in all research groups is exerted by the severity of obesity. This does not depend on the degree of decompensation of carbohydrate metabolism, and only with decompensation with an HbA1c level of more than 10% does the effect of decompensation of carbohydrate metabolism become significant.

According to our analysis of researches of the Russian population, the development of hypogonadism in men with DM2 is associated with macrovascular complications (CHD, DFS, ACVA in anamnesis), which confirms the importance of androgen deficiency in the pathogenesis of atherosclerotic changes in the vascular wall, lipid metabolism disorders [18, 48–50]. In general, modern epidemiological researches clearly indicate the association of low blood testosterone levels with dyslipidemia [51–53]. Men with hypogonadism have a proatherogenic lipoprotein profile with low levels of high-density lipoprotein and high levels of triglycerides and low-density lipoprotein. In our research, we did not assess the lipid profile of patients due to the lack of primary data on these parameters. As for the data obtained on AMI, the absence of significant differences in the incidence of AMI can probably be associated with a high incidence of painless forms of myocardial ischemia and insufficient detection of AMI in connection with this [21].

In addition, the new data on the association of hypogonadism with the development of diabetic neuropathy are available. This is consistent with the few available data that testosterone metabolites, as well as pharmacological agents that increase its level, are neurotropic and are considered by a number of authors as protective agents against diabetic peripheral neuropathy and diabetic encephalopathy [54–55].

Our analysis did not show differences in the incidence of microangiopathy (retinopathy and nephropathy), which probably indicates the absence of a pronounced effect of hypogonadism on the pathogenesis of these diabetic complications.

There were also no significant differences in the hypoglycemic therapy taken.

The limitations of the study

Considering the association of poor control of carbohydrate metabolism and obesity with testosterone deficiency, it can be concluded that the severity of these conditions may affect the incidence of hypogonadism in other samples.

CONCLUSION

The prevalence of male hypogonadism in type 2 diabetes 56.7%. Its development is due to age, obesity, poor control of carbohydrate metabolism. Hypogonadism syndrome is associated with the development of diabetic macroangiopathy and polyneuropathy. Severe violation of glycemic control (HbA1c 10% or more) significantly reduces testosterone production and increases the prevalence of hypogonadism.

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