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NON-DRUG TREATMENT FOR AGE-RELATED HYPOGONADISM IN OVERWEIGHT MEN. LITERATURE REVIEW.

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Introduction: Age-related decrease in testosterone essentially triggers the development of hypogonadism, and it is naturally found in middle-aged and older men. Currently, the number of such patients is about 43%. In studies on male aging in Massachusetts (MMAS-MassachusettsMaleAgingStudy), blood testosterone levels in men aged 40 to 70 years were determined by random sampling, where a total of 1491 men were examined. There was a decrease in the level of total testosterone starting from 30–35 years by 0.8%, and the level of free testosterone by 2% per year. Based on baseline prevalence data by age, it is estimated that approximately 2,4 million men aged 40 to 69 in the United States suffer from androgen deficiency. By these morbidity data approximately 481,000 new cases of androgen deficiency are expected per year in men aged 40–69 in the USA. And these data can undoubtedly be extrapolated to men in other countries and continents.

Aim: to analyze the literature on methods of non-pharmacological correction of age-related hypogonadism in overweight men in Kazakhstan, neighboring countries and the world.

Searchstrategy: literature search was carried out in the electronic databases PubMed, CochraneLibrary, ResearchGate, Webofscience, GoogleScholar, Paragraphmedicine, ScienceDirect and e-library by keywords (age-related hypogonadism, overweight, methods of correction of hypogonadism). 74 relevant works reflecting the characteristics of the problem were selected for description in the review.

Results: The basis of non-drug therapy for age-related decrease in testosterone is an integrated approach. The most promising are adequate physical activity against a background of a balanced diet and minimization of stressful situations. In addition to these basic methods there are other ways of treatment to be suggested: spa therapy and general balneotherapy, correction of concomitant diseases of the organs of the reproductive system (varicocele, hydrocele, exacerbation of chronic prostatitis). With pronounced overweight bariatric surgery is gaining popularity.

Conclusion: With the existing set of methods and techniques used for non-drug correction of age-related hypogonadism, there is no single standard for the management and observation of this category of patients. Such an abundance of applied methods, with all its certain positivity, indicates that there are no methods that could be reliably classified as highly effective in case of androgen deficiency. Therefore, this direction requires further structuring and adaptation to modern requirements by age categories.

Keywords: *age-related hypogonadism in men, overweight, non-drug methods of correction of hypogonadism.*

Резюме

НЕМЕДИКАМЕНТОЗНЫЕ МЕТОДЫ КОРРЕКЦИИ ВОЗРАСТНОГО ГИПОГОНАДИЗМА У МУЖЧИН С ИЗБЫТОЧНЫМ ВЕСОМ. ОБЗОР ЛИТЕРАТУРЫ

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Введение: Важную роль в развитии гипогонадизма играет возрастное снижение тестостерона, и закономерно, что он распространен у мужчин среднего и старшего возраста. В настоящее время количество таких больных составляет около 43%. В исследованиях посвященных проблемам мужского старения в Массачусетсе (MMAS– Massachusetts Male Aging Study), определяли уровень тестостерона в крови у 1491 мужчины в возрасте от 40 до 70 лет методом случайной выборки. Было отмечено снижение уровня общего тестостерона, начиная с 30–35-летнего возраста на 0,8%, а уровня свободного тестостерона – на 2% в год. Исходя из базовых данных о распространенности по возрасту, по оценкам, примерно 2,4 миллиона мужчин в возрасте от 40 до 69 лет в США страдают дефицитом андрогенов. Основываясь на этих данных о заболеваемости, мы можем ожидать приблизительно 481 000 новых случаев дефицита андрогенов в год у мужчин в США в возрасте 40–69 лет. И эти данные, несомненно, можно экстраполировать на мужчин и других стран и континентов.

Цель: анализ литературы о методах немедикаментозной коррекции возрастного гипогонадизма у мужчин с избыточным весом в Казахстане, в странах ближнего зарубежья и мире.

Стратегия поиска: поиск литературы был осуществлен в электронных базах PubMed, CochraneLibrary, ResearchGate, Webofscience, GoogleScholar, Paragraphmedicine, ScienceDirect и e-library по ключевым словам (возрастной гипогонадизм, избыточный вес, методы коррекции гипогонадизма). 74 релевантных работ, отражающих характеристики проблемы были приняты для описания в обзоре.

Результаты: В основе немедикаментозной терапии возрастного снижения тестостерона лежит комплексный подход. Наиболее перспективными являются адекватная физическая нагрузка на фоне сбалансированного питания и минимизация стрессовых ситуации. Дополнением к этим основным методам являются: курортотерапия и общая бальнеотерапия, коррекция сопутствующих заболеваний органов половой системы: варикоцеле, гидроцеле, обострения хронического простатита. При выраженном избыточном весе популярность приобретает бариатрическая хирургия.

Выводы: При существующем множестве способов и методик, используемых для немедикаментозной коррекции возрастного гипогонадизма, нет единого стандарта ведения и наблюдения такой категории больных. Такое обилие применяемых методик при всей своей определенной позитивности свидетельствует о том, что нет методик, которые можно было бы с высокой достоверностью отнести к высокоэффективным при андрогендефиците. Поэтому данное направление требует дальнейшей структуризации и адаптации к современным требованиям по возрастным категориям.

Ключевые слова: *возрастной гипогонадизм у мужчин, избыточный вес, немедикаментозные методы коррекции гипогонадизма.*

Түйіндеме

АРТЫҚ САЛМАҒЫ БАР ЕРЛЕРДЕГІ ЖАСҚА БАЙЛАНЫСТЫ ГИПОГОНАДИЗМДІ ТҮЗЕТУДІҢ МЕДИКАМЕНТОЗДЫ ЕМЕС ӘДІСТЕРІ. ӘДЕБИЕТТЕРДІ ШОЛУ.

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Кіріспе: Гипогонадизмнің дамуында тестостеронның төмендеуі маңызды рөл атқарады, заңдылық бойынша олар орта және егде жастағы ер адамдарда дамиды. Қазіргі уақытта бұндай науқастардың саны 43% жетті. Ер адамдардың қартаюы жөніндегі мәселеге арналған Массачусентс (MMAS –Massachusetts Male Aging Study) зерттеуі барлығы 1491 ерадамның ішінен 40 пен 70 жас аралығындағы ер адамдардың қанындағы тестостерон деңгейін анықтады. 30-35 жасаралығынан бастап жалпы тестостеронның деңгейі 0,8%, ал бос тестостерон деңгейі жылына 2% төмендейтіні анықталды. Жасына, бағасына байланысты алынған жүйелі ақпараттарға жүгіне отырып, АҚШ-ташамамен 2,4 млн ер адамныңішінде 40-69 жасаралығындағы ер адамдар андрогендердің жеткіліксіздігі мен зардап шегеді. Осы ауру жайлы аланған мәліметтерге сүйене отырып, біз АҚШ-та 40-69 жасаралығындағы ер

адамдарда жылына шамамен 481 000 жаңа жағдай андрогендердің жетіспеушілігі бойынша кездесетінін анықтадық. Бұл мәлімет басқада елдермен континенттердің ер адамдарында күмәнсіз кездестіруге болады.

Мақсаты: Қазақстанда, жақын шетелдермен әлемде артық салмағыбар, жасы ұлғайған еркектердегі гипогонадизмді медикаментозды емес әдіспен анализдеп, коррекциялау.

Іздеу стратегиясы: осы кілт сөздер бойынша (жасқа байланысты гипогонадизм, артық салмақ, гипогонадизмді коррекциялау әдісі) PubMed, CochraneLibrary, ResearchGate, Webofscience, GoogleScholar, Paragraphmedicine, ScienceDirect және e-library электронды жүйелерінде әдебиетті іздеу жүргізілді. 74 орынды жұмыстың ішінде мәселені айқындай тын сипаттамалар шолу мақсатында қабылданған.

Нәтижелері: Жас ұлғаюына байланысты тестостеронның төмендеуін медикаментозды емес емдеу негізін де жүйелі тәсілжатыр. Дұрыс тамақтану балансын сақтау және стресстік жағдайларды азайту көрінісінде адекватты физикалық жүктеме ең перспективті болып табылады. Осы негізгі әдіске қосымша ретінде курорттық терапия және жалпы бальнеотерапия, жыныс мүшелерінің қосымша ауруларын: варикоцеле, гидроцеле, созылмалы простатиттің асқынуын коррекциялау болып табылады. Айқын артық салмақ кезінде бариатрикалық хирургия ең танымал.

Қорытынды: жас ұлғаюына байланысты гипогонадизмді медикаментозды емес коррекциялауға арналған әдіс-тәсілдер ішінде бұл категорияда ғы науқастарды қадағалау дабіріккен енгізілетін стандарты әдісі жоқ. Андроген дефициті кезінде қолданылатын барлық әдістероң нәтиже бергенімен, жоғарыэ ффект беретініндәлелдемейді. Сол себепті олар ықарай жас категориясына байланысты заманауи талаптарға сайқұрылымдық және бейімділікті қажететеді.

Негізгі сөздер: *ер адамдардағы жас ұлғаюына байланысты гипогонадизм, артық салмақ, гипогонадизм коррекциясындағы медикаментозды емес әдістері.*

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Introduction

Testosterone is one of the main hormones in the development and maintenance of male vitality [2].The stability of its normal level is vital for the adequate development of the male body and the preservation of male health. Testosterone behavioral effects involve not only the regulation of sexual behavior, but also the desire for competitiveness in everyday life [21,25]. Lack of testosterone in men is invariably accompanied by a decrease in life interests, constant drowsiness, periodic mood swings with a predominance of gloomy and depressed background, which is aggravated by sexual passivity [4,5].

A gradual age-related decrease in testosterone production in men invariably leads to the development of atherosclerosis of the vascular network, which increases the risk of cardiovascular diseases. Studies have confirmed a direct relationship between the level of testosterone in the blood and the level of surrogate points for the development of atherosclerosis [34]. An important component in the progression of hypogonadism is the age-related decrease in testosterone, and it is predictable to be detected in middle-aged and older men. Currently, the number of patients with hypogonadism is about 43 % [32]. The level of free testosterone begins to decrease by 1,2 % per year from the age of 35 [34,38], as for the age of 50-55, the level of total testosterone will decrease by 0.4-1% per year. At this rate, by the age of 80, a man's total testosterone level is about 60 % of his average level at age of 20, and free testosterone is only 20 % [1].

According to the results of a large BACH (Boston Area Community Health) survey conducted in 2002-2005, the prevalence of androgen deficiency was 5.6% nationwide in men aged 30 to 79 years [60].

In studies on male aging in Massachusetts (MMAS-Massachusetts Male Aging Study), blood testosterone levels were determined in men aged 40 to 70 years by random sampling, where 1,491 men were examined. There was a 0.8% decrease in total testosterone levels starting from the age of 30-35, and a 2% decrease in free testosterone levels per year. Based on this incidence data, we can expect approximately 481,000 new cases of androgen deficiency per year in men in the United States aged 40-69 years [18,38].

And this data can certainly be extrapolated to men from other countries and continents [68].

Hypogonadism in older age leads to obesity, osteoporosis, and anemia [26]. Age-related hypogonadism is aggravated and often progresses as a result of overweight [67] leading to obesity, metabolic syndrome, diabetes mellitus, and cardiovascular disease [3,14, 45,61].

Reduced testosterone production, age-related changes in its fraction and metabolism are natural and physiological processes in men, caused by a decrease in serum testosterone levels due to depletion of Leydig cells in the testicles. According to literature data, only 2% of men aged

40-80 years have a true decrease in testosterone. In most cases, concomitant diseases and obesity exacerbate age-related hypogonadism [1,18]. Given the increase in life expectancy of modern men, age-related hypogonadism is becoming increasingly relevant [13,23,47].

Age-related hypogonadism does not have pathognomonic symptoms, so patients with their complaints are observed and treated for a long time by doctors of other specialties (therapists, cardiologists, neurologists and endocrinologists) [9,10]. Doctors demonstrate more and more a lack of awareness in the interpretation and most importantly in diagnosing hypogonadism at the level of primary health care. It is to the PHC doctor that patients first apply to with complaints of general weakness, loss of strength and loss of sexual interest. These complaints are signs of hypogonadism, which can significantly reduce the quality of life. And against this background, there is a need to expand the knowledge of primary care doctors about age-related hypogonadism in older men. To understand the situation, it is necessary to realize that testosterone is not just a sex hormone that is intended to ensure sexual health [45].

Testosterone together with its biologically active metabolites (dihydrotestosterone and estradiol) determine the development and further maintenance of male sexual identity, and the sexual characteristics of the male body [21]. Manifestations of age-related hypogonadism are diverse [53] and therefore doctors of any specialty can meet clinical manifestations of hypogonadism within their specialty [7,8]. Therefore, not only family doctors, but also many doctors of particular specialties (urologists, cardiologists, and endocrinologists) will increasingly encounter in their daily practice the clinical manifestations and symptoms of age-related hypogonadism in men [46]. But currently there are no clear criteria for the management of such patients.

According to the new guideline of the European Association of Urologists (EAU, 2015), male hypogonadism is defined as a clinical syndrome of testosterone deficiency, a low level of which negatively affects the function of most organs and life quality of a man [32,71]. To date, the criteria for diagnosis [22] and replacement therapy for hypogonadism have not been clearly identified. Schemes and methods of drug treatment with testosterone are very diverse, but they raise many questions, both for urologists and patients [42]. Undoubtedly, the rapid effect of such treatment is shown immediately and without apparent difficulties, but the negative aspects of such treatment are often ignored or underestimated [1,25].

A cross-sectional multicenter study conducted in European countries with economies in transition (Poland, Hungary, Estonia) showed a higher prevalence of sexual dysfunction and a correspondingly lower quality of life compared to countries with stable economies (Italy, Belgium, great Britain).

Men in countries with economies in transition reported a higher prevalence of diseases and sexual dysfunction, as well as a lower quality of life. An unstable economy negatively affects sexual health and increases concomitant diseases in men depending on age. So, such state of things indicates that the problem is not strictly medical.

The burden of General and sexual health is higher in countries with economies in transition, which underscores the need to develop more effective strategies to promote healthy aging of men in these countries [27].

Up to 50 years of age, hypogonadism is associated with dysfunction of the hypothalamic-pituitary system and is therefore secondary. In 50-70 years, the decrease in testosterone is basically mixed. After 70 years, hypogonadism is mainly age-related, and therefore the ways to solve this problem should vary depending on the etiology [4].

To date, there is no consensus on what is primary: either hypogonadism leads to the accumulation of visceral fat or overweight leads to a decrease in testosterone due to deposition in adipose tissue [36,37].

In most cases, age-related testosterone decline and midlife crisis coincide in the time of onset and course, which naturally complicates the diagnosis and choice of management tactics. The task of psychologists and urologists is to distinguish between these two concepts that are different in nature and mechanism.Midlife crisis is an isolated psychological problem and has no cardinal connection with a decrease in total testosterone levels. Often, the way the general practitioners identify the midlife crisis with age-related androgen deficiency is erroneous and complicates a diagnosis [54]. The midlife crisis is a purely psychological problem and is not related to the level of serum testosterone [11,54].

Treatment of age-related hypogonadism is aimed at restoring sexual health, adequate libido and enhancing physical condition and, as a result, improving the quality of life in men [6,32,41,63].

Methods of diagnosis and treatment of congenital primary diseases leading to hypogonadism are widely covered in the world literature, while the secondary decrease in testosterone against the background of age is not fully studied.

Ignorance of the etiology and pathogenesis of age-related hypogonadism causes unjustifiably frequent prescription of substitution therapy.

The ultimate goal of treatment for patients with age-related hypogonadism is to increase the level of testosterone in the blood to normal or close to the average. Substitution therapy [20,33] and stimulating therapy of own (endogenous) testosterone are considered to be two main directions in pathogenetic therapy. [14,52].

Testosterone replacement therapy noticeably displays weight loss, reduced waist circumference, and insulin sensitivity. The market for synthetic testosterone is represented by a variety of drugs, but patients are to be monitored constantly, since androgen-dependent symptoms and conditions may develop against the background of therapy [17].

Synthetic testosterone applicationis limited to side effects (liver damage from increased enzymes, risk of prostate cancer) [29,35].

The required level of testosterone in substitution therapy is arduous due to the lack of the currently sufficient data. Experts believe that it is necessary to restore the level of testosterone to the average age indicator, since this level is sufficient to stop the symptoms of hypogonadism. The

treatment regimen depends on the type and form of the drug used [32].

In the US, data on sales of all testosterone products in 41 countries from 2000 to 2011 have been analyzed. 37 countries out of 41 saw significant and progressive growth in testosterone sales over 11 years. The increased use of testosterone appears to be primarily for older men and is due to clinical recommendations that approve the use of testosterone in age-related hypogonadism. Ignoring the fundamental difference between pathological and functional testosterone deficiency, these guidelines tacitly promote increased testosterone prescribing, bypassing the requirement for high-quality clinical evidence of safety and efficacy, and creating a dramatic increase in testosterone drug prescribing. And perhaps this is due to the pharmaceutical lobby [37].

The US food and drug administration claims that there are shortcomings of this therapy and states that the long-term consequences of long-term hormone therapy with testosterone have not been studied. Randomized, placebo-controlled studies are needed on the efficacy and safety of the substitution therapy in men with metabolic syndrome on the background of hypogonadism [30,28,69].

We consider that one of the most preferable ways to solve the problem of age-related androgen deficiency aggravated by overweight might be found in the search for optimally sparing and age-targeted, but at the same time effective methods for correcting the level of testosterone in older men. The search for the new therapeutic and restorative technologies and optimization of the existing ones based on stimulating the body's functional reserves encourage our reviewing new literature data.

The article is **aimed** at analyzing the literature on the non-drug correction methods of age-related hypogonadism in overweight men in Kazakhstan, neighboring countries and the world.

Search strategy. To achieve this goal, we have searched for scientific publications in the databases of evidence-based medicine (PubMed, CochraneLibrary, ResearchGate, Web of Science, GoogleScholar, Paragraphmedicine, ScienceDirect).

Inclusion criteria are as follows: high-quality methodological studies (meta-analyses, systematic reviews, randomized controlled and cohort studies), the results of case-control and cross-sectional studies published with statistically proven conclusions in English and Russian have been also taken into account.

Exclusion criteria involve articles describing an isolated case and personal messages that do not have an evidence base, summaries of reports, abstracts, newspaper articles and advertising articles. Search depth is accounted for 10 years (from 2010 to 2020). We covered 112 papers, and 74 relevant papers reflecting the characteristics of the problem have been accepted for the description in the review.

Keywords for the search were: age-related hypogonadism in men, non-drug correction, overweight, erectile dysfunction

Results

Non-drug therapy for age-related testosterone reduction is based on the comprehensive approach. The most promising methods are adequate physical activity supported with balanced diet and minimizing stressful situations. In addition to these main methods Spa therapy and General balneotherapy, correction of concomitant diseases of the reproductive system such as varicocele, hydrocele, exacerbation of chronic prostatitis are applied. Bariatric surgery is becoming popular with overweight patients.

Bodily exercises

The work by *Lawrence D. Hayes* (2017) who analyzed the effect of moderate aerobic exercise on testosterone in older men, arouse much interest. Objectively, patients reported improved well-being, a certain burst of energy, and better appetite and sleep, but subjectively, the sex gene (SHBG) remained consistently increased in the tests, which keep bioavailable testosterone and free testosterone unchanged compared to the first analysis [39].

Meanwhile, in his research, H. Kumagai (2015) determined the effect of walking and Jogging on endogenous testosterone stimulation. The study involved 44 men, of whom 28 were overweight and 16 were of normal weight. None of the men were engaged in regular physical exercise. All participants were required to take part in an aerobic exercise program, which is 40-60 minutes of walking or jogging 1-3 days a week for 12 weeks. Men's testosterone levels were measured before and after the exercise program. Although the program did not affect testosterone levels in normal-weight men, overweight men showed a significant increase in the hormone level by the end of the 12th week.

Total testosterone levels has increased from 15.4 nmol to 18.1 nmol per liter. The researchers note that testosterone levels in overweight men were still lower than in normal-weight men. They also experienced some weight loss. "Although the degree of weight loss is small, we found that increased physical activity is associated with increased testosterone levels," notes *Hiroshi Kumagai*. [44].

The results obtained have indicated a significant effect of physical exercise on the production of endogenous testosterone in men with an age-related decrease in testosterone. However, the symptoms of obesity require additional stimulation in the form of changes in diet [16].

Nutrition correction

In Spain, 209 men aged 18 to 23 years have been included in an experiment where they studied the effect of diet on sperm parameters and testosterone levels (2015). Two diets have been identified: Mediterranean (characterized by high consumption of vegetables, fruits, and seafood) and Western (characterized by high consumption of processed meat, French fries, and snacks). A direct link has been detected between being overweight and a Western diet. This study has been conducted on healthy and young men, so it is difficult to predict the effect on the ability to fertilize, but the improvement in sperm indicators may indirectly indicate a secondary improvement in the hormonal background. These results have revealed that traditional Mediterranean diets can have a positive impact on male reproductive potential [31].

Joan Khoo evaluated the effect of a low-calorie diet in men with visceral obesity for 8 weeks. According to the results of this study, losing 10% of weight resulted in increased testosterone levels, improved erectile function, and sexual desire. Diet-induced weight loss significantly and rapidly improves sexual function and reduces lower urinary tract symptoms (Luts) in obese middle-aged men with or without diabetes [42].

E. Camacho in 2013 studied the effect of changes in weight and certain life factors on hypothalamic-gonadal function in middle-aged and elderly men. A total of 2,736 men aged 40 to 70 years were examined. In their observations, they noted that a weight loss of at least 10% of the weight showed an increase in testosterone levels by 2.9 nmol/l ($p< 0.01$). This once again confirms the theory that lifestyle and nutrition adjustments that lead to weight loss have a positive effect on serum testosterone levels [23,41].

Bariatric surgery

Recently, bariatric surgery in the correction of obesity has become widespread in the world. *G. Mipdgopei et al.* (2015) stated, that 60 patients with a 35 BMI or more underwent surgery. These patients were severely obese with 2 type diabete. After bariatric surgery, weight loss and controlled sugar stabilization were observed [15,56]. A similar study by *S. Pellitero* (2012) after bariatric surgery for obesity resulted in weight loss and improved testosterone levels [59,72].

However, *J. Himpens* in his work, in the conditions of the University center for obesity in Brussels (Belgium), with laparoscopically regulated gastric banding within 1994 - 1997, after 12 years of observation, noted that only 54.3% had a weight loss of 42.8%. When analyzing long-term data, the author notes that every 3 patients had erosive changes in the stomach, which led to the need for repeated surgery. It is undoubtedly regrettable and requires further research in this direction [40].

Improved sleep

Among men with overweight and metabolic syndrome, there are a lot of people who suffer from night apnea, and who have low serum testosterone levels. Due to apnea, nocturnal hypoxia and a decrease in the level of luteinizing hormone occur. This undoubtedly leads to a decrease in testosterone levels.

R.M. Bercea (2015) and colleagues conducted a study on the relationship between fatigue in night apnea and testosterone levels, and found a relationship: fatigue associated with night apnea was closely associated with low serum testosterone levels. However, this study was conducted on a small group (15 people) and it is very difficult to assess it as a serious study, but this direction can be considered promising for further research [19].

In the experiment by *B. Vlková* (2014), patients suffering from severe sleep disorders in the form of frequent and prolonged apnea were recommended Constant Positive Airway Pressure. This is a method of non-invasive ventilation with constant positive airway pressure using a small compressor and simultaneous monitoring of sleep during treatment. The aim of the study was to analyze and compare the levels of sex hormones in saliva before and after a night of CPAP therapy with night apnea in men and women. The study showed that one night with Constant Positive Airway Pressure (CPAP) therapy does not affect the concentration of testosterone and estradiol in patients with nocturnal apnea, either in plasma or in saliva. In this situation, long-term studies may be necessary to talk about any effectiveness and reliability [71,73] .In this category of patients, the level of testosterone in the blood serum is negatively correlated with the body mass index and the severity of apnea. Measurement of testosterone levels can be an additional useful indicator in the diagnosis of severity and follow-up of patients with obstructive sleep apnea [24]. The relationship between testosterone and nocturnal apnea is complex and not yet fully studied, so apnea can contribute to lower testosterone levels due to hypoxia and sleep fragmentation.

In addition, overweight and old age may be the cause of decreased testosterone secretion in middle-aged men with apnea. Although the effect of apnea correction on testosterone levels remains unclear, treatment of this pathology improves sexual function, especially in men with severe apnea [43,51,57,68].

In addition to the quality of sleep, sleep duration also plays an important role. In their research in 2011*, L. Rachel and Van Cauter* proved that limiting sleep to 5 hours a day leads to a decrease in testosterone levels by 10-15 %. More research is needed on the relationship between sleep and testosterone to determine whether sleep duration should be integrated into the androgen deficiency assessment [32,49]

Thus, improving the quality and duration of sleep has a positive effect on serum testosterone levels, which may provide an additional non-drug alternative to increasing total testosterone. For the category of men with sleep disorders (night shifts, frequent jet lag on a business trip, irregular working hours), it is necessary to take into account when prescribing rehabilitation measures that correct the level of testosterone [21].

Effect of stress

Men with an age-related decrease in testosterone are prone to mood swings and show symptoms of depression. In experimental work on rats in 2011, *R. Steven* evaluated the effect of modulated androgen deficiency (orchoectomy was performed) on the development of depressive-like behavior. The results of the work proved the effect of testosterone levels on resistance to chronic stress in men, therefore, correction of testosterone levels reduces the likelihood of developing possible behavioral or neurological depressive-like conditions in men of these phenotypes [65,66].

Men with hypogonadism are prone to depression. The nature of depressive states is associated with the activity of the hypothalamic - pituitary-adrenal axis, which is subsequently suppressed testosterone. Correction of testosterone levels has an antidepressant effect [70]. Obesity, mainly its abdominal type, is a trigger for the metabolic syndrome and a risk factor for cardiovascular diseases and diabetes. Scientific experiments in recent years have shown more evidently that chronic stressful situations increase the risk of developing abdominal obesity and metabolic syndrome, and this is influenced by the regulatory effects of sex hormones, mainly testosterone. In response to acute stress, perceived as something dangerous for the body's personal safety, a physiological response is often activated to reduce food intake by suppressing appetite. In contrast, chronic stressful situations often force you not to avoid food, but to look for food rich in energy, which contributes to rapid weight gain and leads to obesity.

Stress-related obesity is based on both clinical perspectives and available research conducted on experimental animals. Due to the complexity of neuroendocrine, behavioral, and metabolic adaptation to chronic stress, much more research on this topic is needed to plan specific therapeutic strategies [23,48,58].

Thus, minimizing stressful situations and optimizing your personal life can help increase testosterone levels without the necessary medication. However, it is important to note that the close relationship between stress and testosterone levels remains relevant and requires further research.

Varicocele

Diagnosis and surgical correction of varicocele is relevant for young men as a factor leading to pathospermia and secondary infertility. In older men, the presence of varicocele is ignored, but even if detected, the issue of surgical treatment has never been considered. Although the presence of varicocele for a long time leads to testicular atrophy, which exacerbates hypogonadism. In its meta - analysis, *Fuping Li* notes an improvement in the performance of Leydig cells after surgical treatment of varicocele, which leads to an increase in testosterone levels [50]. Similar works by *Sathya Srini* confirm this theory. Surgery performed to correct varicocele indirectly increases the level of serum testosterone, which leads to an improvement in the sexual function of a man with hypogonadism. Most of the considered works are devoted to the correction of infertility, but the fact of the influence of the operated varicocele on the production of serum testosterone is worth considering to us as part of our search. Therefore, men with age-related hypogonadism should be examined for the presence of varicocele.

But in his work, *Meysam Jangkhah* in a prospective study on 115 men who underwent surgical treatment reports a significant improvement in the quality of sperm, but the level of testosterone has increased slightly. In this direction, further randomized controlled trials are needed to prove a favorable outcome in men with hypogonadism and infertility after varicocelectomy [55].

Varicocelectomy can increase serum testosterone for infertile men with varicocele. Although increasing serum testosterone levels does not necessarily lead to a direct improvement in sperm quality, varicocelectomy can improve hormonal and spermatogenic function [62,64].

Drinking and General balneotherapy

One of the promising directions in non-drug correction of hypogonadism is drinking and General balneotherapy. Regular intake of mineral water improves lipid, water-salt metabolism. Ingestion, coupled with water treatments (herbal bath and circular soul) displays a positive effect on the Central nervous system in emotional terms. Water treatments improve metabolic processes, reduce the level of lipids, and normalize acid balance and electrolyte balance [12].The main method of therapy for men with an age-related decrease in testosterone and obesity is changing lifestyle. The doctor's efforts should be aimed at persistent weight loss. Literature data on this issue show that weight loss has a clear inverse correlation with the level of serum testosterone. Naturally, weight gain leads to a decrease in testosterone.

Numerous studies on this topic indicate that 70% of patients with age-related hypogonadism can restore their own testosterone production without pharmacological correction. Accordingly, this will require normalization of the metabolic processes of a body.

Conclusion

Having analyzed the literature, we came to the conclusion that, in the entire world's problem of age-related hypogonadism in men, against the background of overweight, there are no clear diagnostic criteria, no plan for correcting testosterone deficiency and weight loss, and there is no general consensus on the level of testosterone, no definite answer to whether a stimulating or a drug-replacement therapy is needed.

Among the specialists involved in this issue (urologists, endocrinologists, GP doctors), there is no common understanding of the methods and types of correction of testosterone levels. With the existing set of methods and techniques used for non-drug correction of age-related hypogonadism, there is no single standard for the management and monitoring of this category of patients. Such an abundance of the methods used, for all its certain positivity, indicates that there is no reliable method to be attributed as highly effective in androgendeficiency. Therefore, this direction requires further structuring and adaptation to modern requirements by age categories.

Thus, in the diagnosis and treatment of androgen-deficient conditions against the background of overweight, the search for new research directions for pathogenetic non-drug therapy remains relevant. The use of natural and physical methods to stimulate endogenous testosterone of age-related hypogonadism is a promising direction of modern resource-saving medicine.

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Kuderbaev M.T. - literature search.

Aukenov N.Ye. – general guidance for the research, editing final version of the manuscript.

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