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Andropause – facts and myths

Andropauza – fakty i mity

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Abstract

According to the Polish Menopause and Andropause Society, andropause is a period of the male aging process defined by gradually declining production of androgenic hormones (testosterone and dehydroepiandrosterone), growth hormones and melatonin. The drop in hormone production usually occurs in men over 50 years of age. The symptomatology of these disorders includes gradual deterioration in the quality of life, general well-being and professional performance, libido disorders, sexual dysfunction, intellectual impairment and sleep disturbances. The aim of this paper is to present the pathophysiology of andropause, taking into account the clinical and laboratory diagnostic work-up, available treatment modalities as well as myths about the andropausal period. Since the vast majority of men (several million in Poland) experience systemic changes related to andropause, the topic should be approached holistically, with a proper degree of empathy. A variety of therapeutic modalities are available, which should be employed according to defined principles and contraindications. Unfortunately, a large group of men believe that “this is how it is supposed to be at this age and nothing can be done about it – this is just biology.” This belief, however, is a myth and not a reality. It should be fought against, primarily by raising public awareness, applying prophylactic measures and ultimately through medical interventions.

Keywords: andropause, testosterone, diagnostics, treatment

Streszczenie

Według Polskiego Towarzystwa Menopauzy i Andropauzy andropauza to okres w życiu mężczyzny, któremu towarzyszy pojawienie się postępujących wraz z wiekiem niedoborów hormonów androgenowych, testosteronu i dehydroepiandrosteronu, a także hormonów wzrostu i melatoniny, co następuje zwykle po 50. roku życia. Symptomatologia tych zmian obejmuje stopniowe pogarszanie się jakości życia, ogólnego samopoczucia, sprawności zawodowej, zaburzenia libido, funkcji seksualnych, zmniejszenie sprawności intelektualnej i zaburzenia snu. Celem niniejszego artykułu jest przedstawienie patofizjologii tego okresu, z uwzględnieniem diagnostyki klinicznej i laboratoryjnej, metod terapii, a także mitów związanych z andropauzą. W związku z tym, że zdecydowana większość mężczyzn (w Polsce kilka milionów) ma dolegliwości natury uogólnionej, należy ten temat potraktować holistycznie, z odpowiednią dawką empatii. Możemy się posilować różnymi metodami terapii, które należy stosować zgodnie z określonymi zasadami oraz przeciwwskazaniami. Niestety, duża grupa mężczyzn uważa, że „tak już w tym wieku musi być i nic na to nie poradzimy – po prostu biologia”. I to jest mit, który nie znajduje uzasadnienia – należy z nim walczyć, przede wszystkim poprzez uświadamianie społeczeństwa, stosowanie profilaktyki i na końcu podejmowanie interwencji medycznych.

Słowa kluczowe: andropauza, testosteron, diagnostyka, leczenie

INTRODUCTION

The average male life expectancy in the 1950s was 45 years. However, because of contemporary progress in civilisation – including advances in medicine – the average male life expectancy increased to over 64 years in 2000, and it is expected to reach approximately 75 years in 2050. Consequently, the global population of men older than 65 years will be about 700 million in 2050. At present, the population of men over 50 years of age is approximately 550 million worldwide (including ca. 200 million in Europe). In Poland, there are currently about 4 million men over 50, and 2–2.5 million men over 65 years old. Male aging is characterised by gradual deterioration of physiological functions in multiple body organs and systems including the heart, lungs, kidneys, liver, central nervous system as well as the endocrine system.

The symptomatology of these changes involves steady deterioration of the quality of life and general well-being, impaired work efficiency, sleep disturbances as well as decreased sex drive and sexual performance^(1,2).

WHAT IS ANDROPAUSE?

According to the definition adopted by the Polish Menopause and Andropause Society, andropause is a period of the male aging process defined by gradually declining production of androgenic hormones (testosterone and dehydroepiandrosterone – DHEA), growth hormones and melatonin, typically occurring in men over 50 years of age. The term “andropause” is a rough calque of the term “menopause.” It is thus inherently incorrect, because even in old age men maintain fertility and hormonal function. Women are indeed affected by a physiological “pause,” with the cessation of menstruation and a decline in oestradiol levels virtually to zero, and a significant increase in follicle-stimulating hormone (FSH) resulting from reduced activity of the negative feedback mechanism. However, no changes of this type are seen in men, and the level of testosterone does not always decline. In fact, it is fairly common for men to have testosterone levels at the lower end of normal range. Unfortunately, medical terminology has a number of misleading misnomers, “andropause” (or “male menopause”) being just some of them.

Therefore, a host of other terms referring to this condition have been proposed including:

- PADAM (partial androgen deficiency in aging male syndrome);
- PEDAM (partial endocrine deficiency in aging male syndrome), which highlights a decline in the levels of androgens, DHEA, melatonin and growth hormone;
- secondary hypogonadism;
- AMS (aging male syndrome).

It seems, though, that despite being somewhat misleading and insufficiently accurate, the term “andropause” captures the whole set of endocrine changes affecting elderly men.

The most common andropause-related symptoms include:

- psychological manifestations: mood swings, nervousness, anxiety;
- somatic and vegetative manifestations: general decline in life energy, reduced muscle mass, increased central fat mass, excess respiration, sleep disorders, hypertension, osteopenia, osteoporosis, diabetes;
- sexual manifestations: erectile dysfunction, delayed ejaculation, premature ejaculation, impaired sexual drive;
- the prevalence (in about 30% of men) of disorders including coronary artery disease, hypertension or advanced atherosclerosis which have a negative impact on sexual functioning;
- the need to use drugs (because of urologic disorders, hypertension, gastrointestinal or cardiovascular conditions, depression, etc.) producing adverse effects including erectile dysfunction, of which the patient is usually unaware.

MYTHS ABOUT ANDROPAUSE

1. Penile erection is a sensitive indicator of male sex drive and sexual arousal.
2. The penis must be in full erection during the entire intercourse.
3. Penile erection and ejaculation are closely associated.
4. A man should have an erection “in the blink of an eye.”
5. The quality of sex depends solely on the partner.
6. “Old age will not come alone.”

TESTOSTERONE – MAIN MALE SEX HORMONE

Testosterone is the main male sex hormone which plays a significant role in andropause and is therefore discussed in greater detail below. In men, testosterone is produced primarily by Leydig cells of the testicles, but also by the adrenal glands. Testosterone is synthesised from oestradiol and becomes an active molecule after being released from sex hormone-binding globulins (SHGB).

Active testosterone is only its free fraction, unbound to proteins, accounting for just 1 to 2% of the total amount of the hormone. It is absorbed from the gastrointestinal tract and mucous membranes, more readily from the muscle tissue. The hormone is metabolised in the liver.

Testosterone performs the following functions in the body:

- it is a source of oestradiol (E2);
- it has a direct stimulatory effect on bone cells and fat tissue mass;
- it plays a significant role in the aging process, with levels decreasing with age;
- it stimulates the production of erythropoietin (EPO);
- it promotes the development of male genital organs and male secondary sex characteristics.

Testosterone deficiency in aging men is associated with the processes listed below:

- A decrease in the level of “good” cholesterol (high-density lipoprotein, HDL) and an increase in “bad” cholesterol

levels (low-density lipoprotein, LDL), leading to an elevated risk of coronary artery disease. However, recent pioneering global research challenges the traditional view that the level of HDL should be higher than LDL for a healthy life, showing that both fractions should rather complement (balance out) each other. Since the studies were based on a very limited material, they require further analysis (the findings were announced at one of the conferences as pilot results; they have not been published).

- Coronary artery disease, increased amount of fat tissue.
- Increase in inflammatory processes.
- Increase in the severity of neurological symptoms.
- Increased insulin resistance.

LINK BETWEEN OBESITY AND TESTOSTERONE

A classic symptom potentially occurring in men during andropause may be erectile dysfunction. Also, andropausal men often develop abdominal obesity attributable to an increase in the number of fat cells. This leads to an elevated activity of aromatase, an enzyme inducing the conversion of testosterone into oestradiol. An excess of testosterone inhibits the secretion of luteinising hormone (LH) by the pituitary gland in the mechanism of negative feedback, resulting in the lack of hormonal stimulation of the testes and a significant decline in testosterone levels. This process creates a vicious circle with erectile dysfunction and low testosterone levels increasing erectile dysfunction^(3,4).

Normal testosterone levels are considered to be higher than 11 nmol/L. Hypogonadism is diagnosed when the testosterone level is below 7 nmol/L, while values between 7 and 11 nmol/L require patient monitoring. When performing laboratory evaluation of andropause, account is also taken of the so-called andropause index which captures the biological function, i.e. the ratio of total serum testosterone to luteinising hormone levels (T/LH). The recognised standard range of the andropause index is 1 to 7, while values below 1 may be indicative of hypogonadism⁽⁵⁻⁷⁾.

TESTOSTERONE – RULES OF TREATMENT, DRUG PRODUCTS

Testosterone therapy should be subject to the following restrictions and recommendations.

1. Absolute contraindications: breast cancer (not so uncommon in men!); prostate cancer and hyperplasia [before treatment is started, prostate-specific antigen (PSA) assay and urology consultation are mandatory];
2. Relative contraindications: nephrotic syndrome, migraine of unknown origin, epilepsy, myocardial dysfunction, potential interactions with other drugs (coumarin derivatives!);
3. Adverse effects include allergic reactions, muscle mass gain, inhibition of activity in anterior pituitary lobe, testicular atrophy, gynaecomastia, sleep apnoea, acceleration

of the neoplastic process (e.g. prostate cancer), *polycythemia vera*, liver damage, and kidney failure.

4. Recommendations for patient follow-up during treatment include complete blood counts – CBC (haematocrit, haemoglobin) after 3 months of testosterone treatment, followed by once a year; evaluation of lipid levels every 6 months; evaluation of PSA levels and *per rectum* examination every 6 months; and assessment of treatment outcome every 6 months.
5. Testosterone therapy should be conducted under ongoing supervision of an endocrinologist, urologist and sexologist⁽⁸⁻¹⁰⁾.

Androgen products available in Poland and worldwide:

- oral dosage forms: Proviron 25 mg, Undestor Testocaps 40 mg (standard dosage regimen in Polish patients: 1 tablet 3 times a day), Andriol Testocaps 40 mg, Pantestone 40 mg;
- intramuscular injections: Nebido 1000 mg (every 3 months), Omnadren 250 mg (combination drug – one *i.m.* injection every 3 weeks) Testosteronum Prolongatum Jelfa 100 mg (every 3 weeks, 200 mg), Androtardyl 250 mg, Aveed 750 mg, Depo-Testosterone 200 mg, Sustanon 250 mg (not approved for therapy in Poland), and Testosteron-Depot 250 mg;
- gels, ointments and adhesive patches: Androtop, Androderm, Testavan, Tostran, AndroGel, Fortesta, Testim, Testogel, Vogelxo, Andractim, Testoderm (transdermal scrotal patch)⁽¹¹⁻¹³⁾.

HOLISTIC TREATMENT OF ANDROPAUSE

The management of andropausal patients requires not only medical intervention but also prophylactic measures and appropriate nutrition. Available options include:

- diet rich in micro- and macronutrients (zinc), and vitamins; reduced alcohol consumption and smoking^(14,15);
- daily physical activity;
- prevention of testicular overheating (avoiding tight-fitting trousers, excessively tight underwear, hot baths) and putting laptops on the lap (to prevent the effects of radiation);
- change in the rhythm of sexual activity from the evening to the morning (testosterone levels peak in the morning)⁽¹⁶⁾;
- pharmacological treatment;
- surgical treatment⁽³⁾;
- Renova (low intensity shock wave therapy) – available in Poland⁽¹⁷⁾.

Since the greatest efficacy, both in patients in Poland and worldwide, has been seen with pharmacotherapy, it is discussed in greater detail below. A special focus is put on the treatment with phosphodiesterase type 5 (PDE-5) inhibitors, which represents a therapy of choice in this indication. Other therapeutic modalities include intracavernous injections of vasoactive drugs (alprostadil), adrenergic receptor antagonists (yohimbine), and adjunct drugs (Penigra). The testosterone products used in andropause therapy are described above, while other modalities employed for the treatment of andropausal complaints are discussed in detail in the extensive literature on the topic⁽¹⁸⁻²⁰⁾.

PDE-5 INHIBITORS – MECHANISM OF ACTIVITY, DRUG PRODUCTS

PDE-5 inhibitors act via nitric oxide (NO) in the endothelium. Nitric oxide activates the enzyme guanyl cyclase which converts guanosine monophosphate (GMP) into another transmitter – cyclic guanosine monophosphate (cGMP). The process dilates arterioles in the corpus cavernosum, mediating erection. However, a prerequisite for the efficacy of these drugs is sexual stimulation^(20,21).

Contraindications to the treatment with PDE-5 inhibitors include co-medication with nitrates and molsidomine, past myocardial infarction (within 90 days), unstable coronary artery disease, uncontrolled cardiac arrhythmia, uncontrolled hypertension, cardiomyopathy, past stroke (within 90 days), and blood coagulation disorders^(21,22).

Adverse effects include headaches, dizziness, facial redness, muscle pain, dyspepsia, vision disorders (mainly associated with Viagra treatment – cyanopsia – “blue vision”)⁽²³⁾.

All drugs in this group are metabolised in the liver. As a result, they react with erythromycin, ketoconazole and cimetidine, among other agents. Tablets should not be taken with grapefruit juice⁽²⁴⁾.

All PDE-5 inhibitors exhibit a similar mechanism of action. Differences are only seen in the duration of action (with onset of activity within 15 to 60 minutes, and duration of effect ranging from 6 to 36 hours), and individual patient sensitivity. The most popular PDE-5 inhibitors include: Alsigra, Fildlata, Inventum, Lekap, Maxigra, Maxon, Revatio, Viagra, Vizarsin, sildenafil – various products, Spedra (avanafil), Cialis (tadalafil), Levitra (vardenafil). All the drug products listed above are available in the form of film-coated tablets. Tablet splitting is not recommended, as they crumble easily. They are produced in strengths ranging from 5 mg (for daily use regardless of sexual activity) to 200 mg (for *ad hoc* use before sexual activity)⁽²⁵⁾. It should also be emphasised that a significant proportion of men fall for misleading or false advertisements and purchase so-called “sexual performance enhancing drugs” via a variety of channels. In addition to being ineffective, such agents may even be harmful (some of them have been found to contain mixtures of plaster or ground glass), and produce a potentially catastrophic psychological effect (“I’ve bought this but it does not work!”). It is only after failed attempts at self-treatment that many patients seek professional medical advice. The pattern is very often observed by the author of this paper who is a practising specialist in sexology.

Summing up, it must be stressed that men in their “autumn years” require special medical care. However, based on the advances in contemporary medicine, with the help of a general practitioner, urologist, endocrinologist and sexologist, the process of ageing, as inevitable as it is, may proceed mildly, without a significant adverse effect on the quality of life, thus challenging the traditionally-held belief that andropause is a period in a man’s life when memories prevail over dreams⁽²⁶⁾.

Conflict of interest

The author does not declare any financial or personal links with other persons or organisations that might adversely affect the content of the publication or claim any right to the publication.

References

1. Izdebski Z: Seksualność Polaków na początku XXI wieku – studium badawcze. Wydawnictwo Uniwersytetu Jagiellońskiego, Kraków 2012.
2. Gryżewski A, Pilarski P: Sztuka obsługi penisa. Wydawnictwo Agora, Warszawa 2018.
3. Seifert M, Zdrojewicz Z: Otyłość a zachowania seksualne. Endokrynol Otył Zab Przem Mat 2010; 6: 129–135.
4. Depko A: Otyłość, nadciśnienie tętnicze a dysfunkcje seksualne. Nadciśn Tętn 2009; 13: 139–146.
5. Zdrojewicz Z: Seksualność człowieka w wieku późnej dorosłości. Seria „Biblioteka Nestora”, Vol. IV, Dolnośląski Ośrodek Polityki Społecznej, Wrocław 2011.
6. Zdrojewicz Z (ed.): Miłość, hormony i seks. Wydawnictwo Continuo, Wrocław 2005.
7. Zdrojewicz Z (ed.): Tajemniczy świat kobiecego orgazmu. 2nd ed., Wydawnictwo Continuo, Wrocław 2016.
8. Lew-Starowicz Z: Zaburzenia seksualne w praktyce ogólnolekarskiej. Termedia, Poznań 2004.
9. Zdrojewicz Z: Andropauza – fakty i mity. In: Steciwko A, Mastalerz-Migas A (eds.): Wybrane zagadnienia z praktyki lekarza rodzinnego. Tom 13: Kardiologia, nefrologia, psychologia, pediatria, geriatrya. Wydawnictwo Continuo, Wrocław 2008: 168–177.
10. Lew-Starowicz M, Lew-Starowicz Z, Skrzypulec-Plinta V (eds.): Seksuologia. Wydawnictwo Lekarskie PZWL, 2017.
11. Podlewski J, Chwalibogowska-Podlowska A: Leki współczesnej terapii. 22nd ed., Medical Tribune Polska, Warszawa 2019.
12. Mędraś M: Leczenie testosteronem. MedPharm Polska, Wrocław 2013.
13. Lew-Starowicz Z: O mężczyźnie. Wydawnictwo Czerwone i Czarne, 2012.
14. Szeligowska J, Skorupska E, Mamcarz A: Czy sposób żywienia może wpłynąć na poprawę funkcji seksualnych. Prz Menopauz 2011; 1: 29–36.
15. Zdrojewicz Z, Wiśniewska A: Rola cynku w seksualności mężczyzny. Adv Clin Exp Med 2005; 14: 1295–1300.
16. Zdrojewicz Z: Testosteron – znaczenie kliniczne, zasady terapii. Prz Seksuol 2006; 2, 1 (5): 13–15.
17. Kałka D, Gebala J, Smoliński R et al.: Fała uderzeniowa o niskiej energii w leczeniu zaburzeń erekcji. Seksuol Pol 2018; 16: 20–35.
18. Bancroft J: Seksualność człowieka. Elsevier Urban & Partner, Wrocław 2009.
19. Kempisty-Jeznach E: Książka tylko dla mężczyzn. Prószyński i S-ka, Warszawa 2016.
20. Szczerba K: O penisie prawie wszystko. Przegląd Terapeutyczny 2013; 9–10: 1–3.
21. Zdrojewicz Z: Leksykon seksuologiczny od A do Z. Wydawnictwo Continuo, Wrocław 2012.
22. Darewicz B: Zaburzenia wytrysku i erekcji – możliwości skutecznego leczenia. In: „Zaburzenia seksualne problemem interdyscyplinarnym w medycynie”, Sympozjum naukowo-szkoleniowe Seksuologia 2010, Warszawa: 79–91.
23. Życzkowski M, Bogacki R, Nowakowski K et al.: Chirurgiczne metody leczenia zaburzeń erekcji. Seksuol Pol 2014; 12: 36–42.
24. Zdrojewicz Z, Pachura E, Pachura P: Czy można popijać leki sokiem grejpfrutowym? Fam Med Primary Care Rev 2014; 16: 51–56.
25. Lew-Starowicz Z: Zaburzenia seksualne. Termedia, Poznań 2017.
26. Zdrojewicz Z: Problemy seksuologiczne w endokrynologii. In: Bolanowski M, Kuliczowska-Płakiej J (eds.): Endokrynologia w praktyce klinicznej. Podręcznik dla studentów. Wydawnictwo Uniwersytetu Medycznego we Wrocławiu, 2019.