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Erectile Dysfunction in Young Men: A Growing Medical Problem of the 21st Century - The Literature Review

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ABSTRACT

Introduction: Sexual functioning is an important aspect of health that affects quality of life. Erectile dysfunction (ED) is a condition in which a man is unable to achieve or maintain an erection sufficient for satisfactory sexual intercourse. ED is a common problem, and research shows that it is increasingly affecting young men. Although ED is associated with men over 40, the increase in the number of younger men reporting ED suggests that the problem is becoming more common. ED has a significant impact on men's social interactions and overall well-being. In this review, we are focused on the increasing male problem with ED - epidemiology, diagnosis, and treatment of it.

Materials and Methods: This article reviews literature incorporating data from PubMed using keywords such as 'erectile dysfunction', 'PDE5 inhibitors', 'PIED'

Summary: Erectile dysfunction among men under 40 is an increasingly rapidly growing problem today. Men with ED report decreased life satisfaction and poor interpersonal relationships. Sexual function affects men's well-being. In order to diagnose, thorough diagnostics should be performed, which includes a medical interview and physical examination, sexual function assessment questionnaires, laboratory tests, and imaging. Each patient should be assessed individually. Erectile dysfunction is typically divided by its cause: organic, psychogenic or combination of both. However, this classification should be used with caution as most cases are actually of mixed etiology.

Conclusion: Nowadays, the treatment for ED offers many more or less invasive options. Physicians must be aware that there is no single treatment that fits all patients or all situations.

Keywords: erectile dysfunction, PDE5 inhibitors, hypogonadism, PIED, intracavernosal injection, pharmacological treatments; regenerative strategies; surgical strategies; vacuum erection device

Introduction

Erectile dysfunction (ED) is a growing problem among men under 40. Studies show that it is becoming increasingly common among young men in Poland. Despite available therapies, many men avoid seeking help, which highlights the need for education and campaigns to reduce the stigma surrounding sexual health. ED is most often associated with older men, but the problem is increasingly related to young men. Traditional factors that once explained male sexual problems, such as diabetes mellitus (DM), cardiovascular diseases (CVD), and psychogenic factors, seem insufficient to explain the rapid increase in erectile dysfunction in men under 40. Although psychogenic factors remain the most common cause of ED, attention should be focused on the possible etiology underlying porn-related sexual dysfunction. Most patients with ED can be treated appropriately after a basic diagnostic evaluation, which includes

a detailed medical interview including the topic of sexual life, a physical examination, and laboratory tests.

Epidemiology

Based on the current ED studies published in 2023, it can be seen that in the entire population in Poland, the incidence of erectile dysfunction ranged from 30.1% to 61.1%, depending on the definition and diagnostic methods used. Although the incidence increases with age, the data also indicate a significant increase in cases among young men. Studies show that 17% of men under 40 have experienced erection problems in at least one sexual initiation. In this age group, ED occurs in both sporadic and chronic forms. Despite this, only 15% of young men reported to a specialist because of ED, which demonstrates the low level of awareness and reluctance to seek medical assistance among young men [1]. For comparison, a systematic review from 2002 found that the prevalence of ED in men under 40 years of age was approximately 2%. Although pooling data across studies is difficult because of methodological differences in the magnitude of the increase, this is a significant and independent approach to epidemiological trends [2].

Etiology

ED is commonly classified as either psychogenic or organic. Psychogenic ED has been linked to factors such as depression, stress, generalized anxiety, or fear of developing ED. At the same time, organic ED has been attributed to physical conditions—neurological, hormonal, anatomical, or pharmacological side effects [3, 5]. In men under 40, psychogenic ED is the most common diagnosis. Researchers estimated that only 15%–20% of cases are of organic origin [3, 4]. Psychogenic conditions are often associated with couple misunderstandings, as well as problems related to work, which can often affect sexual desire. Even the occurrence of initial episodes of ED, as well as other sexual dysfunctions, can lead to performance anxiety and thus to an evasive reaction to avoid failure [3]. Among organic diseases, endocrine disorders such as hypogonadism play a significant role. Hyperprolactinemia also affects sexual desire, and therefore is related; Finally, hypothyroidism can occur due to hyperprolactinemia from

hypothyroidism [6]. The psychiatric cause, from the remains of depression, which is the inability to "feel pleasure" and a mood set on sadness, is the cause of ED [3]. Other infections of the disease system can cause deterioration of the quality of life and thus entail the risk of disease. Another condition can stem from vascular, metabolic, neurological, inflammatory and iatrogenic causes [3]. Diabetes affects 20-25% of men with erectile dysfunction, and dyslipidemia in 40-70% [7, 8]. Neurogenic causes, such as multiple sclerosis, Parkinson's disease, and spinal cord injuries can lead to organic erectile dysfunction. [9, 11] Symptomatic patients undergoing radiotherapy and radical pelvic surgery (i.e., radical prostatectomy) have a high risk of developing cavernous nerves with subsequent neurogenic ED. Mechanical conditions are the main source of fibrosis, caused by induration plasticity of the penis (IPP) or after penile trauma. In patients infected with male accessory gland infection (MAGI) and presenting ED, dilatation of the periprostatic venous plexus has been shown [11, 12]. The appearance has also been reported to be a consequence of preceding COVID-19. There are even some categories, such as antiandrogenic drugs, H2 antagonists, ACE inhibitors, and psychotropic drugs, that may be ED through mechanisms that are not fully understood [11]. Traditional factors that once explained men's sexual problems appear insufficient to explain the dramatic increase in erectile dysfunction in men under the age of 40. Alterations in the brain's motivational system are being investigated as a possible etiology underlying pornography-related sexual dysfunctions [2, 3]. This review also considers evidence that the unique properties of Internet pornography (unlimited novelty, potential for easy escalation to more extreme material, video format, etc.) may be strong enough to condition sexual arousal to aspects of Internet pornography use that do not transfer easily to real-life partners, such that sex with desired partners may not register as fulfilling expectations and arousal declines [3,10]. Clinical reports suggest that cessation of Internet pornography use is sometimes sufficient to reverse negative effects, emphasizing the need for large-scale studies using methodologies that require subjects to control for the variable of Internet pornography exposure [3].

Diagnostic

The evaluation of a man with erectile dysfunction includes three categories: history and physical examination, laboratory tests, and additional imaging tests. Every patient reporting a sexual problem should have an interview and physical examination. Risk factors for ED should always be considered. An assessment to differentiate between organic and psychological causes

of ED is essential. During the visit, the severity, onset, and duration of ED should be assessed. The assessment should also include a psychosocial assessment, as ED and its treatment are related to overall quality of life, relationships, self-confidence, self-esteem, and depression. It should be remembered that disease can be both a cause and a result of ED [13,15].

Medical History and Physical Examination

The medical history should include age, sexual orientation, marital status, and sexual history. Information should be collected on the onset and duration of erectile dysfunction, the occurrence of morning erections, and whether treatment has been undertaken. An important aspect is also erection on sexual stimulation or masturbation, lifestyle, relationship with a partner, and sexual desire [13, 14]. Questionnaires should be used to assess erectile function and determine the potential effects of treatment. The SHIM is one of the most commonly used tools to assess the severity of ED. The SHIM consists of five questions based on a five-point Likert scale and is derived from the IIEF 15-question gold standard [9]. The IIEF has high sensitivity and specificity in detecting treatment effects, but its length makes it ineffective for use in the office setting, whereas the SHIM is specifically designed as an office screening tool for ED [13, 16,17]. In the SHIM score, lower scores predict worse ED with a classification into five severity levels: no ED (SHIM score 22–25), mild (17–21), mild to moderate (12–16), moderate (8–11), and severe (1–7). Physical examination may be helpful in the presence of comorbidities associated with ED, such as testicular size and consistency, and other conditions [18], including hypertension [19] and arrhythmia [20]. Physical examination in men with ED is recommended but not always necessary, according to the International Consultation on Sexual Medicine (ICSM) [21]. The examination should also assess secondary sexual characteristics, peripheral pulse and sensation, abdominal masses, and the presence of gynecomastia. Waist and hip circumference can help assess obesity, while the waist-to-hip ratio is a good indicator of weight loss and response to hypogonadal therapy [22], and a digital rectal examination is recommended for men considering hormone therapy.

Laboratory tests

Laboratory tests focus on assessing risk factors for ED and, according to ICSM recommendations, include tests assessing the hypothalamic-pituitary-gonadal axis, lipid status, and glucose metabolism (HbA1C). Assessment of the hypothalamic-pituitary-gonadal axis may

reveal endocrinopathies that can significantly affect erectile function, including hypogonadism [13, 23]. Given the similarity of symptoms between hypothyroidism and hypogonadism and the impact of hypothyroidism on hypogonadism, thyroid function tests should be considered if the clinical situation requires them [24, 25]. It should be noted that ICSM recommends performing these tests, but it is not always necessary. The choice of laboratory tests should be made on a case-by-case basis [13].

Additional tests

While the history, physical examination, and laboratory tests are sufficient to diagnose most physical causes of ED, in some patients, additional diagnostic tests may identify a specific etiology of ED and help guide treatment choices.

Psychophysiological Evaluation

The distinction between psychogenic and organic ED can be made without invasive testing using the nocturnal penile tumescence (NPT) test. The NPT test measures the number, duration, and stiffness of tumescence episodes during sleep [13]. The test is usually performed at the patient's home on a minimum of two consecutive nights. Normal erectile function is considered to be at least one episode of >60% penile tip stiffness lasting no less than 10 minutes. However, given the overall complexity of the test, it is not recommended for routine evaluation of the ED. That said, the degree of psychogenic involvement can be easily deciphered by using a thorough sexual history that assesses the quality of erection upon awakening, as well as during masturbation, foreplay, and intercourse [26]. When erectile function varies as a function of circumstances, psychogenic ED can be accurately diagnosed. In contrast, men with organic ED are more likely to have persistent erectile difficulties

Vascular evaluation

Specialist vascular evaluation aims to diagnose arterial and venous insufficiency in men with ED. Penile double-sonography, which combines ICI with Doppler ultrasonography to assess the direction and velocity of blood flow, is the most common and informative method for assessing both arterial insufficiency and veno-occlusive dysfunction [13, 30]. Men with arteriogenic ED demonstrate a peak systolic velocity (PSV) of <25 ml/s, which has 100% sensitivity and 95% specificity in men with abnormal pudendal arteriograms. Venocclusive

dysfunction, in contrast, demonstrates a PSV of 25 ml/s or greater but with a sustained end-diastolic velocity (EDV) of >5 ml/s, with a sensitivity of 90% and specificity of 56% for venous leakage on penile cavernosometry [13, 31]. The vascular resistance index (RI) ($RI = PSV - EDV / PSV$) is a measure of vascular resistance based on the Doppler spectrum, with an RI of ≥ 0.9 indicating normal function and a value of ≤ 0.75 indicating venous leakage [13, 28, 29, 81]. Arteriography can help define arterial obstruction, although it is more appropriate for assessing anatomy than function, and is most useful in young men with traumatic arterial rupture or perineal compression injury to plan surgical reconstruction. In ED, the iliac, internal pudendal, penile, and inferior epigastric arteries are examined [9, 27].

Treatment

Treatment of ED, according to the guidelines of the European Society of Urology, includes the use of phosphodiesterase type 5 (PDE5) inhibitors, vacuum erection devices (VED), and low-intensity extracorporeal shock wave therapy (Li-ESWT). In refractory cases, intraurethral injections or surgical procedures are used. ED treatment should be tailored to the patient's needs and take into account efficacy, safety, tolerability, and individual patient preferences. To adapt the treatment, the cause of ED should be taken into account. Depending on whether the cause is primary, the cause should be eliminated, which may lead to the elimination of ED [32]. However, if the cause of ED is different, the following are suggestions for treating patients.

Patient Education

The first method of treating ED may be patient education, which involves informing patients about psychological processes and physiological aspects of sexuality so that the patient can understand their problem. Therefore, consultation with the patient should include a discussion about the needs and expectations of the patient and his partner [33].

Modifiable risk factors

ED may be associated with modifiable or reversible risk factors. The patient's lifestyle and medications should be taken into account. ED may also be associated with the patient's diseases, such as endocrine or metabolic disorders, such as diabetes, and cardiovascular problems, such

as hypertension. Some studies indicate that lifestyle changes such as physical activity, weight loss, or treatment of CVD risk factors can improve sexual function in men with ED [9, 32].

Phosphodiesterase type 5 inhibitors

Four selective PDE5 inhibitors have been approved for the treatment of ED. Their efficacy has been confirmed in almost every subgroup of patients with ED. Efficacy is defined as an erection in which the penile rigidity is sufficient for satisfactory intercourse. The choice of PDE5 inhibitor depends mainly on the frequency of sexual intercourse and the patient's personal preferences [9, 32].

Sildenafil

Sildenafil is administered in doses of 25, 50, and 100 mg, and the recommended starting dose is 50 mg. The dose should be adjusted according to the patient's response and side effects. The window of efficacy is 30-60 minutes after administration, up to 12 hours. In a 24-week dose-response study, 25, 50, and 100 mg improved erectile function by 56%, 77%, and 84%, respectively, in men with ED compared to 25% in patients taking a placebo [9,32,34,35].

Tadalafil

Tadalafil is administered in occasional doses of 10 and 20 mg or in a daily dose of 5 mg. The recommended starting dose is 10 mg and should be adjusted according to patient response and side effects. The window of efficacy ranges from 30 minutes after administration to 36 hours, with maximum efficacy achieved after about 2 hours. In a 12-week dose-response study, improved erectile function was reported by 67% and 81% of men with ED taking 10 and 20 mg of tadalafil, respectively, compared to 35% taking a placebo [9,32,36].

Vardenafil

Vardenafil is administered at on-demand doses of 5, 10, and 20 mg. The recommended starting dose is 10 mg and should be adjusted according to patient response and side effects. Vardenafil is effective 30 minutes after administration. In a 12-week dose-response study, improved erectile function was reported by 66%, 76%, and 80% of men with ED taking 5, 10, and 20 mg of vardenafil, respectively, compared with 30% of men taking a placebo [9,32,37].

Avanafil

Avanafil is administered in on-demand doses of 50, 100, and 200 mg. The recommended starting dose is 100 mg taken as needed 15 to 30 minutes before sexual activity, and the dose may be adjusted based on efficacy and tolerability. In the general ED population, the mean percentage of sexual attempts that resulted in intercourse was 47%, 58%, and 59% for the 50, 100, and 200 mg groups compared with 28% for the placebo group [9, 32, 38].

Current recommendations are to try all PDE5 inhibitors (one at a time) before moving on to more invasive therapy.

In patients with ED who are not responding to PDE5 inhibitor therapy, the physician should ensure that the medication is prescribed and used correctly by the patient. Absorption of sildenafil, vardenafil, and avanafil may be delayed by high-fat meals. Care should be taken to ensure that patients do not wait too long or too soon after taking the medication before attempting intercourse [9,32].

To date, there are no data available from double- or triple-blind multicenter studies comparing the efficacy and/or patient preferences of sildenafil, tadalafil, vardenafil, and avanafil. The choice of medication will depend on the frequency of intercourse (occasional use or regular therapy, three to four times per week) and the patient's personal experience. Patients need to know whether the medication is short-acting or long-acting, what its possible drawbacks are, and how to use it [39].

Intracavernosal injection

The intracavernosal injection (ICI) of vasoactive agents like papaverine and prostaglandin E1 represents a significant advancement in erectile dysfunction treatment and can also serve as a diagnostic tool [40]. ICI is an effective local drug therapy for ED, and individual treatment plans can be formulated according to the individual conditions and needs of patients [41]. Combining various vasoactive drugs and adjusting their dosages can greatly enhance treatment effectiveness while minimizing complications. Research has shown that patients receiving a combination of papaverine and prostaglandin E1 experienced better erectile function compared to those treated with prostaglandin E1 alone [42]. However, with the use of PDE5 inhibitors, the clinical use of ICI has gradually declined because it has a high dropout rate and is associated

with priapism, ecchymosis, hematoma, and penile fibrosis [43]. Currently, the combination of ICI and Doppler ultrasonography is mainly used in the diagnosis of ED and the assessment of penile hemodynamics [44].

Hormone Replacement Therapy

Androgen plays an important role in promoting normal penis growth and stimulating secondary sexual characteristics in men. Androgen is mainly secreted by the testicles, androgen deficiency leads to a series of pathophysiological conditions that damage sexual function and overall body health [45]. In the clinic, androgen replacement therapy can restore serum testosterone levels to normal and improve sexual desire in patients with hypogonadism [46]. More importantly, androgen replacement therapy in combination with PDE5 inhibitors can effectively treat ED, and patients' erectile function can be maintained even long after discontinuing the medication [47].

Vacuum erection device

The vacuum erection device (VED) is a mechanical tool that enhances blood flow to the corpora cavernosa by generating a vacuum pressure of up to 250 mmHg. A constriction ring placed at the base of the penis helps sustain the engorgement and supports erection [48]. VED is primarily employed in the treatment of organic erectile dysfunction and is known for its effectiveness and minimal side effects [49].

Penile prosthesis implantation

Implantation of a penile prosthesis (PPI) is currently considered a third-line therapy for erectile dysfunction. Because it can cause irreversible damage to the smooth muscle of the corpora cavernosa, it is usually considered when oral PDE5 inhibitors, intracavernous injections, and VED therapy are ineffective [50]. The 3-piece inflatable prosthesis is currently the most commonly used implant and is also the most satisfactory [51]. The three-piece inflatable prosthesis allows manual control over the penis's thickness, length, and rigidity, effectively mimicking the natural erection process. An early multicenter study showed that more than 90% of ED patients and their partners could achieve normal sexual activity after receiving a penile prosthesis implant [52]. However, PPI is expensive, traumatic, and prone to complications such

as prosthesis infection, pump migration, automatic pumping, secondary surgery, etc. Therefore, PPI is not considered a first-line therapy. [53].

Low-intensity extracorporeal shock wave

Low-voltage extracorporeal shock wave (Li-ESW) is a physical shock wave that emits an energy density of less than 0.1 mJ/mm². Li-ESW, as a noninvasive therapeutic technique, directs sound waves to the target tissue by penetrating through the tissue structure [54]. Research indicates that reduced blood flow in the corpus cavernosum is a contributing factor to erectile dysfunction (ED). Li-ESW has been shown to enhance the expression of eNOS, VEGF, and other angiogenic factors within the corpus cavernosum, leading to blood vessel dilation, the formation of new blood vessels, improved circulation, and enhanced erectile function [55, 56]. Li-ESW is a promising treatment method for refractory ED. It can restore the function of the penile endothelium and increase the blood flow through the corpus cavernosum. Nevertheless, the exact therapeutic mechanism of Li-ESW remains unclear and requires further investigation and study.

Summary

Erectile dysfunction is increasingly affecting young men and should be recognized as an important public health concern. The diagnosis of erectile dysfunction is the result of comorbidities, primarily from the circulatory system. Information about the patient with erectile dysfunction can be appropriately treated after basic diagnostics, which consists of detailed information on the topics of daily life, physical examination, and research on the topic. While PDE5 inhibitors remain the first-line therapy, alternative treatments such as hormone therapy, vacuum devices, intracavernosal injections, or penile implants may be necessary. Novel therapies like low-intensity shockwave therapy and regenerative strategies hold promise, but require further research. Physicians must be aware that no one treatment applies to all patients or all situations. Further research into the molecular mechanisms of ED and the development of improved results on ED and its conclusions will further expand the information arsenal of current treatment, improving not only the quality of life of these men but also their life expectancy.

Disclosure

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