



Review Article

Erectile Dysfunction: A Comprehensive Review on Recent Advancement

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ABSTRACT

In the world today, erectile dysfunction (ED) is a serious health problem that significantly lowers both the quality of life and the level of happiness of both the affected person and his spouse. The male sexual health treatment paradigm for ED has recently evolved from a psychosexual model to a new model that includes oral and intracavernosal injection pharmacotherapy, vacuum constriction devices, and penile prostheses. This evolution has been made possible by recent advances in basic sciences. This development has occurred at the same time that our awareness of male sexual health issues has grown. Epidemiological evidence demonstrates the pervasiveness of these issues and identifies the significant morbidity they cause, both for individuals and relationships. In this study, we looked into the most recent ED studies and revised treatments.


INTRODUCTION

According to epidemiological research, erectile dysfunction, or ED, is a highly frequent disorder in males between the ages of 40 and 70. ED is the chronic inability to create or maintain a penile erection that is stiff enough to achieve a fulfilling sexual intercourse. Up to 52% of them are impacted by this issue, which lowers their quality of life. [1] The hydraulic effect of blood entering and staying in the sponge-like bodies within the

penis causes a penile erection. Diabetes, cardiovascular illness, brain disorders (such as the trauma from prostatectomy surgery), hormonal issues (hypogonadism), and pharmacological side effects are the most significant organic aetiologies. Erectile dysfunction can be linked to relationship issues and negative perceptions of men in general, which has serious psychological repercussions [2].

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Early historical accounts of this clinical illness include references to men having a poor penile erection in more than 5000-year-old Egyptian texts [3]. Assuming that these were the primary causes of this problem, managing ED focused mostly on psychosocial or hormonal variables. Psychoanalysis, hormonal therapy, and sex therapy were the most common treatment modalities. If these managements did not succeed, further tactics were employed, ranging from mechanical devices to herbal supplements thought to improve sexual performance. If these managements did not succeed, further tactics were employed, ranging from mechanical devices to herbal supplements thought to improve sexual performance. In other words, early penile implants developed in the 1950s and vacuum-pump technology developed in the late 1960s were confirmed to produce penile rigidity, eliminating the need for comprehensive understanding or practical application of the physiology or biochemical characteristics of the erectile response.

PATHOPHYSIOLOGY

An erection of the penis is a neurovascular phenomena that needs dilatation of the penile vasculature, relaxation of smooth muscles, and maintenance of normal veno-occlusive activities. The most frequent underlying cause of organic ED is penile vascular disorders, which can involve a number of pathophysiological mechanisms, including impaired arterial inflow, impaired smooth-muscle relaxation in the cavernosa, increased cavernosal smooth-muscle contraction brought on by chronic ischaemia, cavernosal fibrosis, veno-occlusive dysfunction, and chronic or intermittent hypoxemia. For many cases of ED, endothelial dysfunction is the common route. [7] ED can be a precursor to different types of cardiovascular issues as well as an early sign of widespread endothelial dysfunction. When analysed, it was shown that 40% of men with ED

who have no cardiac symptoms nevertheless had severe coronary artery disease. About 50% of these men also have an abnormal stress test. The primary risk factors for vascular diseases are those other than age (lack of exercise, diabetes, smoking, hypertension, abnormal lipid profile and obesity). In general, ED can be caused by any disease that impairs endothelial function. Endocrine issues and depression are other contributing factors.

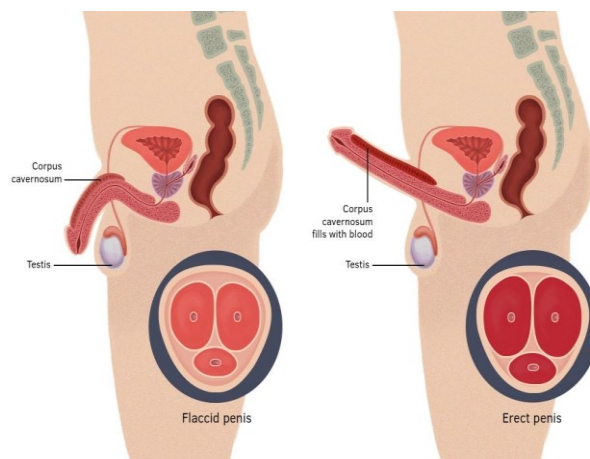


Fig 1: Spectrum of Erectile Dysfunction

Psychogenic

- Performance anxiety
- Loss of attraction
- Relationship difficulties
- Stress

Psychiatric

- Depression

Neurogenic

- Spinal cord injury
- Pelvic surgery
- Pelvic radiotherapy
- Multiple sclerosis
- Diabetes mellitus
- Intervertebral disc lesion
- Alcohol

Endocrine

- Hormonal deficiency
- Testosterone deficiency
- Raised sex hormone-binding globulin

Hyperprolactinaemia

Arteriogenic

Hypertension
Smoking
Diabetes mellitus
Hyperlipidaemia
Peripheral vascular disease
Metabolic syndrome

Venous

Functional impairment of the veno-occlusive mechanism

Drugs

Central and/or direct effect, most commonly

Antihypertensives
Antidepressants
Luteinizing hormone releasing hormone analogues

DIAGNOSIS

A thorough anamnestic investigation (onset of ED, time from onset, correlation with a particular partner, couple conflicts, erection/rigidity, ejaculation without erection, nocturnal spontaneous erections) and specific questionnaires (i.e., International Index of Erectile Function- IIEF 15 (ED: total score 26) or- IIEF 5 (ED: total score 22) should be used to determine the presence and severity According to the IIEF score, there are several levels of impairment (mild, moderate, and severe) [12]. A specialised assessment of the neurogenic reflex as well as first- and second-level first-level (hormonal and biochemical) and second-level (penile colour Doppler, monitoring of nocturnal penile erections) tests may also be recommended. The psychosexual approach is obviously crucial. Additionally, 10% of people who are sexually healthy may experience periodic or persistent periods of trouble achieving or sustaining an erection [13]. This may be brought on by sexual discomfort followed by performance anxiety; in these cases, the notion of subclinical erectile dysfunction has been proposed [14].

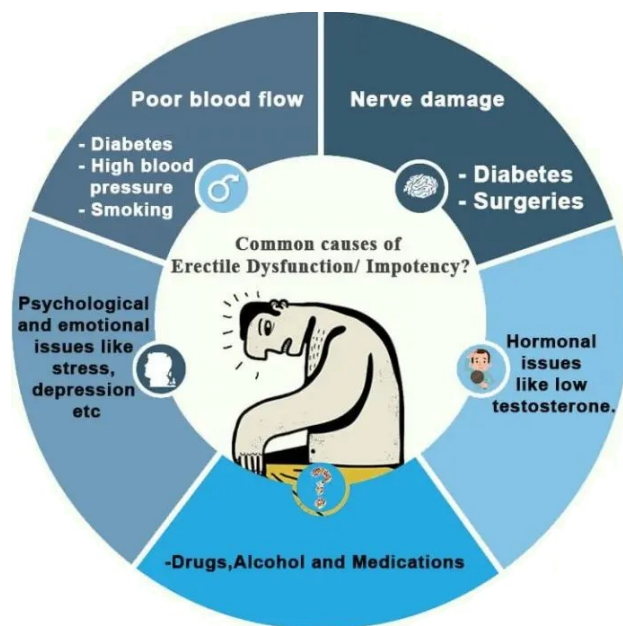


Fig 2: Common causes of Erectile dysfunction

TREATMENT

Alchemy and aphrodisiacs were used as ED treatments in earlier eras. The pan-psycho theory put forward by Freud was first put forth around the turn of the 20th century. So, up until the 1970s, administering androgens was the only option other than psychotherapy. Right now, altering one's lifestyle is a crucial treatment strategy. The second strategy focuses on treating recognised etiopathogenic causes when it is practical. When endocrine and metabolic diseases are taken into account, testosterone replacement therapy is used to rectify hypogonadism. Additionally, hypo- or hyperthyroidism should be treated, as well as hyperprolactinemia. Regaining acceptable sexual performance also depends on controlling the lipid/metabolic profile. The interference of medications with the erectile mechanism or with sexual desire is a particularly problematic condition, especially when the substance cannot be stopped or replaced. In order to promote the recreational and hedonistic element of sexuality in situations of relational and intrapsychic reasons, it

is obvious that the psychosexual method is still useful and essential.

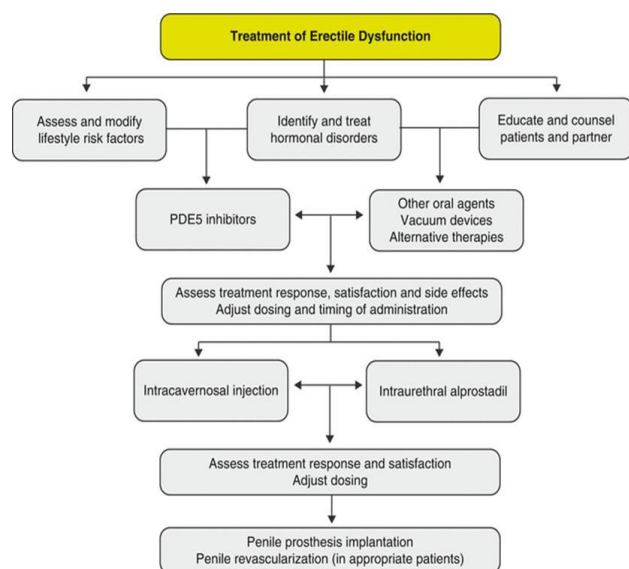


Fig 3: Current treatments of erectile dysfunction

PDE5-i Treatment

The primary method of treating erectile dysfunction is with oral PDE5-Is (phosphodiesterase type 5 inhibitors). The use of penile devices, testosterone therapy, injectable therapies, lifestyle changes, and counselling are other treatments. [9-11]. There are 11 different PDE isoenzymes that are expressed in diverse tissues of the body in varying amounts. Although it is present everywhere, the PDE5 enzyme is more common in penile tissue. The enzyme PDE6, which is present in high quantities in the retinal rod and cone photoreceptors, is mildly inhibited by sildenafil in addition to PDE5 inhibition, presumably resulting in a mild impairment of colour discrimination [17]. Because of this, the initial PDE5i was referred to as the "blue pill."

Psychosexual, couple, and partner therapy

When serious psychological issues are identified, psychosexual treatment is advised. Men with mostly psychogenic erectile dysfunction benefit the most from it. Sensate concentration, sex

education, and interpersonal therapy are examples of methods used in psychosexual therapy.

Nutraceuticals

Several randomised controlled studies on the use of nutraceuticals (ginseng, saffron, Tribulus terrestris, Pinus pinaster, and Lepidium meyenii) or dietary supplements in patients with ED were examined in a recent meta-analysis [22]. L-citrulline and L-arginine have also been suggested as dietary supplements for ED. Each of them seems to slightly boost NO production, however the exact mechanism of action is yet unknown [23]. Before definite conclusions can be formed, however, bigger and better investigations are needed [24].

Lifestyle modification

altering one's way of life Recent fundamental and clinical investigations have revealed that addressing a number of lifestyle variables, including obesity, smoking, alcohol use, and insufficient physical exercise, that are frequently linked to erectile dysfunction can significantly enhance erectile functioning. [12-15] According to Mannino et al. [16], men who stopped smoking had a lower risk of erectile dysfunction than those who were still smoking. Guay et al. [17] observed that individuals who had smoked more than 30 pack-years saw a considerable and quick improvement in their erectile function after quitting (calculated by multiplying the number of cigarette packs a person smokes per day by the total number of years this person smoked; i.e., 30 packyears means the person smoked a pack of cigarettes every day for 30 years). The current body of published research is not quite certain if drinking alcohol negatively impacts erectile function. [15, 18, 19] In a different trial, 110 obese men with erectile dysfunction were randomised to receive either a comprehensive weight management programme that included food counselling and exercise instruction, or only educational assistance on weight loss. When

compared to the latter group, the former group had considerably less body weight, engaged in more physical activity, and had a significant improvement in their erectile dysfunction ratings after two years. Later research provided more evidence to support these findings. [20, 21] Although current research shows that changing specific lifestyle choices might significantly improve erectile dysfunction in males, definitive results cannot be drawn without numerous carefully planned, prospective, and sizable controlled studies. Additionally, according to the current research, changing one's lifestyle may improve one's erectile function, but only after at least two years, which is a considerable amount of time. On the other hand, after three months, a combination strategy of oral PDE5-Is and lifestyle changes might enhance the outcomes. [23] In addition, effective erectile dysfunction medications should not be stopped while making lifestyle changes.

Psychosexual therapy

Due to the fact that each patient's anxiety comes from a different place, psychosexual treatment for ED cannot be standardised. Relationship issues, melancholy, guilt, intimacy issues, and a lack of sexual experiences can all lead to an increase in anxiety and/or conflict, which can ultimately lead to ED. Psychosexual therapies can range from straightforward sex education to better relationship communication to cognitive and behavioural therapy, and they are frequently used in conjunction with ED medication. The short-term effects of psychosexual treatment are comparatively positive, but the long-term effects are poor. [24, 25]

Pharmacotherapy

The majority of ED patients will react to the current crop of safe, efficient oral pharmaceuticals. These include sildenafil, tadalafil, and vardenafil, which are PDE5 inhibitors. other medical procedures, including:

Vacuum devices and intracavernosal medications are used "on demand," but their dropout rates are high due to side effects, a fear of needles, and the partner's reluctance to participate. A significant majority of patients experience both organic and psychogenic ED. Organic ED may be accompanied with performance anxiety that develops over time, significantly impairing erectile function. The doctor and psychotherapist may need to work together and include counselling with physical treatment, such taking an oral pharmaceutical drug, in order to treat these guys holistically.

Pharmacological treatment

Oral pharmaceutical treatment PDE5 inhibitors are a highly effective medication for ED. The PDE5 inhibitors specifically block PDE5 and increase the amount of cGMP available for relaxing smooth muscles, causing vasodilatation, boosting corporal blood flow, and promoting erection. Numerous studies demonstrated the effectiveness, safety, and tolerability of the potent, competitive on-demand PDE5 inhibitor medications sildenafil (Viagra, Pfizer, Inc., New York, NY, USA), tadalafil (Cialis, Eli Lilly and Company, Indianapolis, IN, USA), and vardenafil (Levitra, Bayer Schering, Pharma AG, Leverkusen, Germany), as well as a daily dose of [26-28]. The overall effectiveness of the various PDE5 inhibitors seems to be comparable, with 65-70% of the males finishing a sexual encounter. Effectiveness is correlated with the degree and severity of ED, and it has been shown that individuals with severe vascular ED, diabetic ED, and post-radical prostatectomy ED have much lower effectiveness. Data show that the pharmacokinetic characteristics, effectiveness, potency, half-life, and side effect profiles of sildenafil, tadalafil, and vardenafil vary. Foods heavy in fat slow down and diminish the absorption of sildenafil and vardenafil, but they have no impact on the pace or volume of tadalafil absorption. The half-lives of sildenafil, vardenafil,

and tadalafil are 4-5 h and 17.5 h, respectively, whereas the mean time to maximum plasma concentration for sildenafil and vardenafil is 1 h and for tadalafil is 2 h. Tadalafil (Cialis 2.5, 5 and 10 mg) can be considered first-line therapy, especially in men who frequently engage in intercourse or prioritise spontaneity of sexual intercourse as a key treatment objective. Daily dosing of tadalafil produces efficacy and side-effect rates comparable to those of on-demand application of the highest doses of either tadalafil or other PDE 5 inhibitors. [29] The endothelial function and/or erectile function may both be improved or restored with daily dosage.

Intracavernosal injection (ICI) therapy

Treatment for ED with ICI therapy along with vasodilator medications, such as papaverine and phentolamine alone or in combination with alprostadil (Caverject Impulse, Pfizer), which relaxes the arterial and trabecular smooth muscle, is successful. [30] Most men who struggle with ED can benefit from ICI treatment, although it works best for those who don't react to oral medication. [31]

Vacuum constriction devices

By applying a vacuum to the penis inside of a vacuum cylinder, the vacuum constriction device induces tumescence and stiffness, which is maintained by a constricting ring at the base of the penis. Simply put, blood is trapped in the penis' intra- and extracorporeal compartments distal to the constricting ring.

Surgical treatment

Surgery has only been used to treat ED in individuals who have failed or are contraindicated for conservative therapy. The majority of these individuals will have severe Peyronie disease, penile corpus cavernosum fibrosis, or venous or arterial disorders. Although some individuals may benefit more from surgical intervention, there is a far higher rate of morbidity and problems than with medicinal therapy.

CONCLUSION

A prevalent issue, ED is frequently linked to a worse quality of life for both the patient and their spouse. Risk factors for ED include smoking, hypertension, hyperlipidemia, diabetes mellitus, and hypertension. ED is a predictor of overall cardiovascular health and silent myocardial infarctions and may be the earliest sign of widespread endothelial dysfunction. Most men can improve and/or restore their sexual functioning with the help of ED medication alone or in conjunction with graded psychosexual therapy.

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