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Dolna 17, Warsaw,
Poland 00-773
+48 226 0 227 03
editorial_office@rsglobal.pl

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COMPREHENSIVE REVIEW OF TREATMENT OPTIONS FOR ERECTILE DYSFUNCTION: MODERN AND TRADITIONAL METHODS

Oskar Sienkiel *(Corresponding Author, Email: sienkieloskar@gamil.com)*
7th Naval Hospital in Gdańsk, Gdańsk, Poland
ORCID ID: 0009-0002-4524-0721

Agnieszka Fitas
4th Clinical University Hospital in Lublin, Lublin, Poland
ORCID ID: 0009-0005-9285-9174

Wojciech Gąska
Stefan Cardinal Wyszyński Provincial Specialist Hospital SPZOZ in Lublin, Lublin, Poland
ORCID ID: 0009-0005-7621-3533

Julia Głowacka
Stefan Cardinal Wyszyński Provincial Specialist Hospital SPZOZ in Lublin, Lublin, Poland
ORCID ID: 0009-0004-3262-5598

Mathias Spitaleri
7th Naval Hospital in Gdańsk, Gdańsk, Poland
ORCID ID: 0009-0007-0293-1764

Filip Kieloch
1st Clinical University Hospital in Lublin, Lublin, Poland
ORCID ID: 0009-0003-5116-9703

Dawid Sewruk
Stefan Cardinal Wyszyński Provincial Specialist Hospital SPZOZ in Lublin, Lublin, Poland
ORCID ID: 0009-0008-4153-7126

Wiktor Gąska
University Clinical Centre in Gdańsk, Gdańsk, Poland
ORCID ID: 0009-0003-8818-988X

Karol Kanon
University Clinical Centre in Gdańsk, Gdańsk, Poland
ORCID ID: 0000-0001-6705-1302

Karolina Dębek-Kalinowska
Stefan Cardinal Wyszyński Provincial Specialist Hospital SPZOZ in Lublin, Lublin, Poland
ORCID ID: 0000-0001-9931-6002

ABSTRACT

Introduction: Erectile dysfunction (ED), or impotence, is a condition where a man can't get or keep an erection firm enough for satisfying sexual intercourse. It affects men of all ages and is caused by a variety of physical, psychological, or social factors. The number of ED cases is growing annually, and treatment costs are rising steadily. This combination of increasing prevalence and rising expenses highlights the need for a highly optimized treatment method. Efforts should focus on finding a solution that is as effective as possible while also being cost-efficient. The goal is to provide accessible, high-quality care without the financial burden, ensuring that men who suffer from this condition can find relief and improve their quality of life. The search for such a method is crucial given the growing impact of ED on men worldwide.
Aim: The aim of this study was to review literature studies on ED and methods for treating this condition.
Method: Data for the article were retrieved by using Pub Med setting the time descriptor to 2020-2025.
Conclusions: Despite the availability of many effective treatments for erectile dysfunction (ED), it can still be a challenging condition due to the variety of underlying causes. Therefore, an individualized approach and thorough diagnostics are essential. Regenerative therapies and shockwave therapy, although still experimental, offer new therapeutic opportunities. In the future, it will be important to conduct randomized studies with long-term follow-up to assess the effectiveness and safety of these new methods.

KEYWORDS

Erectile Dysfunction, Phosphodiesterase 5 Inhibitor, Intracavernosal Injection, Vacuum Erection Device, Penile Prosthesis, Stem Cell, Extracorporeal Shock Wave

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Introduction

According to the definition, erectile dysfunction (ED) is the persistent inability of the penis to achieve and maintain an erection sufficient for satisfactory and effective sexual intercourse [1]. This disorder is a common problem among men and affects all age groups.

Despite the challenges related to a clear definition and epidemiology of ED, a significant increase in the number of cases has been observed for many years [2]. Currently, around 320 million men worldwide are living with ED. Over the course of their lives, more than 50% of men experience erection problems, which can significantly affect their mental well-being [2,3].

The likelihood of developing ED is clearly correlated with age, ranging from approximately 5–15% in men under the age of 40 to about 50–70% in men aged 40–70, depending on the sources [4].

ED is a condition with a highly diverse etiology and numerous risk factors, including physiological ones such as: diabetes, obesity, cardiovascular diseases, benign prostatic hyperplasia, multiple sclerosis (MS), smoking, penis surgery and injuries. There are also psychosocial risk factors, such as: depression, schizophrenia, chronic stress, and genophobia [5–9].

Additionally, according to recent studies, widespread use of social media and pornography is suspected to be a possible contributing factor [10].

PDE5 Inhibitors

Thanks to sexual stimulation, nitric oxide (NO) is released by endothelial cells and non-adrenergic neurons into the corpora cavernosa of the penis. This, in turn, activates the enzyme guanylyl cyclase, which is responsible for converting guanosine triphosphate (GTP) into cyclic guanosine monophosphate (cGMP).

The release of cGMP leads to the relaxation of smooth muscle in the blood vessels of the penis. As a result, there is a significant increase in blood flow to the penis, leading to an erection. Phosphodiesterase type

5 (PDE5) is the most common subtype of PDE found in the smooth muscle of the penis. This enzyme is responsible for breaking down cGMP, which in turn leads to the end of the erection [11,12].

The action of PDE5 inhibitors is based on blocking the breakdown of cGMP, which makes the erection more efficient and longer-lasting. It is important to note that drugs from this group do not cure ED; they only temporarily improve erectile function. Moreover, PDE5 inhibitors require the presence of sexual stimulation to be effective [13].

Drugs in this group include sildenafil, tadalafil, vardenafil, and avanafil. Individual drugs differ in onset and duration of action, as well as in their selectivity. Tadalafil and vardenafil have a longer duration of action, up to 36 hours. Avanafil, one of the newer drugs in this group, is characterized by a rapid onset (it starts working after about 15 minutes) and a short duration of action [14,15,16].

Sildenafil, the best-known and earliest widely used drug, has a medium duration of action of about 4 hours. Its standard dose for treating this condition is 50 mg [17]. PDE5 inhibitors are considered first-line treatment for ED. However, it is important to remember that they act only symptomatically, and their use does not lead to a permanent cure for ED [17].

In addition, their use may be associated with various side effects, such as headache, flushing, visual disturbances, hemophilia, cardiovascular conditions (including aneurysms), and indigestion [18,19].

Intracavernosal injections (ICI)

Intracavernosal injections (ICI) involve administering medication directly into the corpora cavernosa of the penis. This is one of the treatment methods for erectile dysfunction (ED). The most commonly used drugs for these injections are prostaglandin E1 derivatives, such as alprostadil. Less frequently, medications like papaverine or phentolamine are used due to a higher risk of side effects.

The mechanism of action of drugs used in ICI involves the dilation of blood vessels in the penis and increased blood flow, leading to an erection. One advantage of this therapeutic approach is that patients can administer the injection themselves after prior training by a urologist [22].

ICI is often used in cases where PDE5 inhibitors are ineffective. In a recent study conducted this year involving 308 men—of whom 96% had failed therapy with PDE5 inhibitors and 66% had also failed VED treatment—the benefits and drawbacks of using alprostadil in ICI were evaluated.

Of the 308 men, 182 (59%) found ICI to be an effective treatment for ED. The study results indicate a high efficacy of ICI with alprostadil in patients who did not respond to PDE5 inhibitors and VED therapy.

However, the same study reported a relatively high rate of side effects associated with ICI. Local pain occurred in 12% of patients, and priapism (a painful, prolonged erection) was observed in 1%. The most common side effect was facial flushing, which occurred in 69 patients (22.5%) [23].

Vacuum Erection Devices -VED

A vacuum erection device (VED) is a mechanical tool that supports erection by creating a vacuum. The device consists of a cylinder placed over the penis and a pump that removes air from the cylinder, generating negative pressure of up to 250 mmHg. This vacuum draws blood into the corpora cavernosa of the penis, leading to its enlargement and rigidity.

Once an erection is achieved, a constriction ring is placed at the base of the penis to maintain blood flow and prevent venous outflow, allowing for sexual intercourse [20].

VED is an effective and relatively safe device for use. In a 2021 study involving 56 participants with an average age of 64, both patient and partner satisfaction with the device was evaluated. Patients were educated, given detailed instructions, and monitored throughout their use of the device.

The study showed that 96% of patients confirmed the device's effectiveness in maintaining an erection, and 100% said they would recommend it to others. Additionally, 84% of female partners reported more enjoyable sexual experiences.

However, 23% of patients experienced physical discomfort while using the device, most commonly associated with pain caused by the constriction ring [21].

Penile prosthesis implantation (PPI)

Penile prosthesis implantation (PPI) is considered a third-line treatment for erectile dysfunction (ED). It involves the surgical insertion of either malleable or inflatable implants that restore the ability to achieve an erection. Currently, the most commonly used device is the three-piece inflatable prosthesis. This method is typically reserved for men with severe ED who have not achieved satisfactory results with other treatments.

Because it is a surgical procedure, thorough clinical and psychological assessment is essential prior to implantation. This includes a detailed medical history and physical examination, psychological counseling, and comprehensive patient education. Infection control—both local (in the perineal area) and systemic—is especially important, as infections are a primary contraindication for PPI.

Advances in technology and surgical techniques have significantly reduced the rate of postoperative complications, although they still pose challenges for urologists. The most common complications associated with PPI include infection, improperly sized cylinders, migration of the scrotal pump, urinary retention, and penile shortening [24].

Despite the potential risks and contraindications, PPI remains an excellent alternative for carefully selected patients with ED. A recent study showed that the vast majority of patients who underwent PPI were satisfied with the treatment outcomes, and complications—mainly infections controlled with antibiotic therapy within a week—occurred in only 5% of cases [25].

Low-intensity extracorporeal shock wave (Li-ESWT)

Low-intensity extracorporeal shockwave therapy (Li-ESW) involves the use of acoustic waves characterized by high-pressure amplitudes. A standard shockwave lithotripter system consists of three main components: a shockwave generator, a localization system for accurately identifying and targeting the treatment area, and a positioning mechanism that aligns the targeted tissue within the focal zone of the wave. Additionally, a coupling pad with conductive gel ensures effective transmission of shockwaves from the generator to the patient's tissues.

There are three main types of shockwave generators: electrohydraulic, electromagnetic, and piezoelectric. Acoustic shockwaves differ from commonly used ultrasound waves in that they operate at a lower frequency.

Li-ESW works by inducing microtrauma in the targeted tissue. These micro-injuries stimulate the release of vascular endothelial growth factor (VEGF) and nitric oxide (NO), both of which are key mediators in angiogenesis. This process promotes neovascularization and vasculogenesis within the penile tissue, ultimately enhancing blood flow and improving erectile function.

The optimal number of shocks per Li-ESW session is between 1,500 and 2,000, with energy levels typically ranging from 0.10 to 0.13 mJ/mm² [26].

Meta-analyses have shown that Li-ESW significantly improves scores on the International Index of Erectile Function (IIEF) and the Erection Hardness Score (EHS) in patients with ED. Given its high efficacy and minimally invasive nature, Li-ESW is rapidly gaining popularity as a promising treatment option [27, 28].

Stem cell injection therapy

Stem cells have the ability to differentiate into various cell types, a process made possible by the influence of complex environmental factors and cytokines. Depending on the extent of their developmental potential, they can be classified as totipotent, pluripotent, multipotent, or unipotent [29].

Preclinical studies primarily focus on the use of different types of stem cells (e.g., mesenchymal, adipose-derived, umbilical cord, or bone marrow) in rat models of erectile dysfunction (ED). These therapies lead to improved erectile function mainly through paracrine mechanisms—such as the release of factors that support tissue regeneration and enhance blood flow—rather than direct differentiation of the stem cells into penile tissue.

More recent studies are exploring the combination of stem cell therapies with genetic modifications, neurotrophic proteins, or tissue engineering materials, achieving a synergistic effect and enhanced efficacy. However, it is still unclear whether these complex modifications offer superior results compared to stem cells alone.

Despite numerous studies demonstrating the effectiveness of stem cell therapy in rodents with ED, there is a lack of data from advanced clinical trials in men. The latest review papers include nine studies involving a total of fewer than 100 male ED patients. These are phase 1 and 2 trials, with follow-up periods ranging from 6 to 62 months.

The findings clearly confirm the effectiveness of intrapenile stem cell therapy. Moreover, no serious adverse effects have been observed in the participants. The main limitation of this therapeutic approach remains the small number of subjects studied [30, 31].

Summary

Erectile dysfunction (ED) is a prevalent condition affecting men across all age groups, characterized by the persistent inability to achieve or maintain an erection sufficient for satisfactory sexual performance. Its multifactorial etiology includes both physiological and psychosocial risk factors, with prevalence increasing significantly with age.

Traditional first-line treatment relies on phosphodiesterase type 5 inhibitors (PDE5i), which enhance erectile function symptomatically by preventing the degradation of cGMP, though they require sexual stimulation and do not address the underlying causes of ED.

Alternative therapeutic options for patients unresponsive to PDE5i include intracavernosal injections (ICI), vacuum erection devices (VED), and penile prosthesis implantation (PPI). ICI, particularly with alprostadil, has shown high efficacy but comes with a notable rate of side effects. VEDs are non-invasive and highly effective, with high satisfaction rates among patients and their partners, although they may cause discomfort. PPI remains a viable option for severe or treatment-resistant cases, offering long-term satisfaction despite being invasive and associated with surgical risks.

Innovative approaches such as low-intensity extracorporeal shock wave therapy (Li-ESWT) and stem cell injection therapy are emerging as promising strategies. Li-ESWT stimulates angiogenesis through microtrauma-induced release of growth factors, significantly improving erectile function in a non-invasive manner. Stem cell therapy, particularly using mesenchymal or adipose-derived stem cells, demonstrates regenerative potential through paracrine effects and tissue repair.

Although preclinical studies show encouraging results, clinical trials in humans remain limited in size and scope. In conclusion, while conventional treatments for ED are well-established, novel therapies such as Li-ESWT and stem cell injection offer promising alternatives that may address the underlying pathophysiology of ED. Further large-scale clinical trials are essential to validate their safety, efficacy, and long-term outcomes in diverse patient populations.

Disclosures

Conceptualization: Oskar Sienkiel, Karolina Dębek-Kalinowska
Methodology: Wojciech Gąska, Karolina Dębek-Kalinowska
Software: Dawid Sewruk, Julia Głowacka
Check: Dawid Sewruk, Wiktor Gąska
Formal analysis: Julia Głowacka, Filip Kieloch
Investigation: Wojciech Gąska
Resources: Filip Kieloch, Wiktor Gąska
Data curation: Julia Głowacka
Writing - rough preparation: Oskar Sienkiel, Mathias Spitaleri
Writing - review and editing: Mathias Spitaleri, Karol Kanon
Visualization: Karol Kanon, Agnieszka Fitas
Supervision: Oskar Sienkiel
Project administration; Filip Kieloch, Karol Kanon

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