Pathogenesis and treatment of diabetes mellitus-related erectile dysfunction: current therapies and potential challenges

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Abstract
Erectile dysfunction (ED) is one of the important complications of diabetes, which is very common in diabetic patients, affecting more than half of male patients, and the incidence of the disease is about 3.5 times that of the normal population. The pathogenesis of diabetic erectile dysfunction (DMED) is complex, involving nerve, vascular, endocrine, muscular and psychological aspects. At present, the therapeutic approaches of DMED include drug therapy, surgery, physical therapy and so on. This article provides a review of current research on the pathogenesis and treatment of DMED. Further elucidation of the pathogenesis of DMED and the development of new therapeutic approaches are of great significance for the prevention and treatment of DMED.

Keywords: diabetes mellitus (DM); erectile dysfunction (ED); pathogenesis; therapies

Acknowledgments
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Abbreviations
DM: Diabetes mellitus; SD, sexual dysfunction; ED, erectile dysfunction; DMED, diabetes mellitus-related erectile dysfunction; AGEs, advanced glycation end products; NO, nitric oxide; ET-1, endothelin-1; cGMP, cyclic guanosine monophosphate; NOS, nitric oxide synthase; C43, connexin43; NADPH, nicotinamide adenine dinucleotide phosphate; nNOS, nitric oxide synthase; iNOS, inducible nitric oxide synthase; sGC, guanylate cyclase; GTP, guanosine triphosphate; Smc1, smooth muscle cells; PPI, penile prosthesis implantation; PDE-5, phosphodiesterase type 5; VCD, vacuum compression device; LI-ESWT, low-energy extracorporeal shock wave therapy.

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**Background**

Diabetes mellitus (DM) is a chronic metabolic disease characterized by elevated blood glucose levels. In recent years, the morbidity and prevalence of DM have shown an upward trend, and its complications have become a serious threat to public health. These complications include macrovascular disease, microvascular disease, and neuropathy. DM is also an important cause of male sexual dysfunction (SD), including erectile dysfunction (ED), sexual desire disorder, ejaculation dysfunction and lack of orgasm, of which diabetic erectile dysfunction (DMED) is the most important type, its pathogenesis is complex, involving nerve, vascular, endocrine, muscular and psychological aspects [1]. According to statistics, by 2023, the number of DM patients worldwide will exceed 592 million [2]. Additionally, ED is a common issue among diabetic patients, affecting over half of male patients, with a prevalence rate approximately 3.5 times higher than that of the normal population [3]. Given the high occurrence of DMED in diabetic patients and its impact on quality of life, this review aims to provide a comprehensive overview and discussion of the pathogenesis and treatment of diabetic erectile dysfunction with a view to informing clinical practice.

**Modern medicine’s understanding of the pathophysiologic mechanisms of DMED**

Erection is a complex physiological process that involves the coordinated activity of multiple brain regions, the spinal cord, and peripheral nerves. It exemplifies the intricate interplay between the central nervous system and peripheral tissues, which is essential for maintaining erectile function. Autonomic nerves (sympathetic and parasympathetic nerves) and somatic nerves (sensory and motor nerves) control penile erection. Signals from the brain and tactile stimulation of the genitals can activate the erectile process by regulating the spinal erectile centers located at T11-L2 and S2-S4. Additionally, hormonal levels can affect central activity and activate the erectile process. Following the input of nerve impulses, neurotransmitters are released, resulting in the relaxation of the smooth muscle of the corpus cavernosum, increased arterial blood flow, decreased venous return, increased intrapenile pressure, and increased blood volume, ultimately leading to an erection [4, 5]. The occurrence of DMED is closely related to various factors, including blood vessels, nerves, corpora cavernosa smooth muscle and tunica albuginea, endocrine system, and even social and psychological factors.

**Vascular factors**

DM can cause macrovascular and microvascular disease, which in turn affects the blood supply to the penis. Macrovascular abnormalities can lead to atherosclerotic narrowing and micro arterial occlusion of the penile arteries, resulting in arterial hypertension and inadequate corporal artery function, leading to inadequate blood flow to the penis. Microvascular disease can disrupt the closing ability of the venous plexus in the corpus cavernosum, leading to insufficient blood flow and ultimately triggering ED [6]. In DM patients, abnormalities in glucose and lipid metabolism, increased blood viscosity, and the generation of advanced glycation end products (AGEs) can damage blood vessel walls. AGEs can interfere with the synthesis of vascular collagen, which can cause damage to the vascular wall. This damage can lead to abnormal changes in vascular function and structure, and even the formation of plaques or blood clots [7]. These factors can alter penile hemodynamics and lead to ED [6, 8, 9]. Additionally, vascular endothelial cell dysfunction is also an important factor. Endothelial cells produce nitric oxide (NO) and endothelin-1 (ET-1), which regulate the contraction and relaxation of smooth muscle cells. In a hyperglycemic state, excessive oxygen radicals cause oxidative damage to cells and inhibit the synthesis of nitric oxide (NO). Meanwhile, plasma endothelin-1 (ET-1) levels are elevated in patients with DM, which can lead to abnormal relaxation of smooth muscle cells and ED [10, 11]. The reduction of NO can also decrease cyclic guanosine monophosphate (cGMP) in cavernosal tissue, leading to dysfunction in smooth muscle cell relaxation [12].

**Neural factors**

It has been suggested that abnormal glucose metabolism may induce oxidative stress in neurons, as abnormal glucose metabolism can cause neuropathy through multiple pathways [13], leading to sensory nerve conduction dysfunction in the perineum [14]. Additionally, autonomic nerves that innervate penile blood vessels, such as adrenergic and cholinergic nerves, can be damaged, resulting in an imbalance of arteriovenous contraction in penile erection and the formation of venous leakage, which can cause ED [15]. Reduced or absent parasympathetic activity can lead to increased norepinephrine levels, inhibition of nitric oxide synthase (NOS), reduced secretion of neurogenic NO and further exacerbation of smooth muscle relaxation dysfunction [16].

**Damage of corpus cavernosum smooth muscle and tunica albuginea**

In addition to endothelial factor disorders that lead to abnormal relaxation of corporal smooth muscle, hyperglycemia can also lead to smooth muscle atrophy and collagen deposition [17]. Hyperglycemia may modify the expression of connexin43 (Cx43) and P2 purinoceptor (P2R) subtypes in the rat corpora cavernosa and bladder, which can alter the permeability of gap junctions [18]. The content of α-actin in the smooth muscle tissue of the corpora cavernosa of streptozotocin-induced diabetic rats is significantly reduced [19]. Abnormal glucose metabolism can cause tunica albuginea fibrosis, leading to penile malformation and abnormal blood flow, resulting in ED [20].

**Endocrine factors**

Penile erectile function is influenced by the endocrine gland hormones in the body, and DM can lead to hypogonadism [10, 21]. The persistent hyperglycemia induced by DM will affect the physiological function of the hypothalamic-pituitary-gonadal axis, resulting in the release of gonadotropin, reduced serum testosterone synthesis, and endothelial cell dysfunction leading to erectile dysfunction [22, 23]. Androgens also play a crucial role in maintaining the structure and function of the peripheral nerve network, the structural integrity of the cavernous body, the tunica albuginea, and the endothelium of the cavernous cavity [24]. The decline in serum testosterone levels among DM patients may exacerbate lesions affecting these tissues.

**Social psychological factors**

DM is a metabolic disease that requires lifelong treatment, and its various complications, including ED, bring great psychological pressure and economic burden to patients. The incidence of depression in patients with DM is twice that of patients without DM [25], and the risk of ED in men with DM who exhibit depressive symptoms is more than six times higher than that in men with DM who do not have depressive symptoms [26]. Therefore, psychosocial factors play an important role in the occurrence of ED in DM patients, and psychological counseling should be regarded as an effective tool for the treatment of DMED [27].

**Factors related to NOS-Mediated signaling pathways**

Nitric oxide synthase (NOS) is a crucial enzyme responsible for the production of the key signaling molecule NO. Its activation is closely linked to the relaxation of corpus cavernosum smooth muscle cells and blood vessels, constituting a classical signaling pathway that regulates penile erection. NOS is widely present in various tissues and organs of the human body and exists in three different isoforms: neutral nitric oxide synthase (nNOS), inducible nitric oxide synthase (iNOS), and endothelial nitric oxide synthase (eNOS). With the involvement of oxygen (O2) and nicotinamide adenine dinucleotide phosphate (NADPH), NOS catalyzes the conversion of L-arginine to guanidino acid, producing NO in the process. NOS is primarily found in the nervous system. When the body is sexually stimulated, the
parasympathetic nerves and cavernous nerves can produce neuronal NO through eNOS, activating guanylate cyclase (sGC) to catalyze guanosine triphosphate (GTP) into cyclic guanosine monophosphate (cGMP). This leads to an increase in intracellular cGMP, promoting the relaxation of smooth muscle cells (SMCs), dilation of sinusoids, and increased arterial blood flow, resulting in penile erection. eNOS is mainly located in vascular endothelial cells and is responsible for catalyzing the production of most NO. eNOS-derived NO helps maintain normal blood pressure and blood flow. During penile erection, eNOS-generated NO further enhances vasodilation, leading to sinusoidal congestion and increased intracavernosal pressure, which is crucial for maintaining erection [28]. iNOS is not normally expressed in cells but can be induced by inflammatory mediators, cytokines, and other factors. Once expressed, iNOS can continuously activate and efficiently produce large amounts of NO, with much higher efficiency compared to nNOS and eNOS [29]. However, iNOS-derived NO is typically associated with inflammatory responses and cellular damage, which may lead to vasoconstrictive responses and affect penile erectile function (Table 1). In the bodily environment of diabetics, multiple related pathways will be affected, further affecting vascular function and erectile function (Table 2).

**Treatment of DMED**

The treatment of DMED should be based on active control of blood glucose, and the hypoglycemic regimen should follow the principle of individualization. In view of the variety and complexity of the etiology of DMED, it is necessary to choose the appropriate treatment method based on the specific condition of the patient, and the patient's personal experience and preferences after treatment should be fully considered. At present, oral drugs are considered the first-line treatment for DMED, including phosphodiesterase type 5 (PDE-5) inhibitors, dopamine receptor agonists, and testosterone replacement therapy. Invasive medical treatments such as penile cavernous injection and urethral suppository therapy are considered second-line treatments.

### Table 1 Effects of NOS subtypes on penile erection

<table>
<thead>
<tr>
<th>NOS subtype</th>
<th>Expression location</th>
<th>Activating factors</th>
<th>Main role</th>
<th>Impact on penile erection</th>
</tr>
</thead>
<tbody>
<tr>
<td>nNOS</td>
<td>Nervous System</td>
<td>Sexual Stimulation, Parasympathetic Nerve Activity, Cavernous Nerve Stimulation</td>
<td>Produces neuronal NO, activates signal pathway in smooth muscle cells</td>
<td>Initiates erection process, promotes smooth muscle relaxation and increased blood flow</td>
</tr>
<tr>
<td>eNOS</td>
<td>Vascular Endothelial Cells</td>
<td>Shear Stress of Blood Flow, Sexual Stimulation</td>
<td>Catalyzes the production of NO, promotes vasodilation</td>
<td>Enhances vasodilation, maintains erection</td>
</tr>
<tr>
<td>iNOS</td>
<td>Various Cells (Inducible Expression)</td>
<td>Inflammatory Mediators, Cytokines</td>
<td>Efficiently produces large amounts of NO, may lead to vasoconstrictive responses</td>
<td>May affect erectile function during inflammatory responses, usually detrimental to erection maintenance</td>
</tr>
</tbody>
</table>

### Table 2 The impact of diabetes on NOS-Related pathways

<table>
<thead>
<tr>
<th>Pathway/Factor</th>
<th>Normal mechanism</th>
<th>Impact of diabetes on the pathway</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Polyols pathway</td>
<td>NADPH is involved in various cellular metabolic processes.</td>
<td>In diabetes, the polyol pathway is activated, leading to excessive consumption of NADPH, which inhibits NO synthesis and reduces NO synthesis. Additionally, increased polyol pathway activity accelerates the formation of AGEs, which bind to eNOS and inhibit its function, further reducing NO synthesis and causing endothelial damage.</td>
<td>[30]</td>
</tr>
<tr>
<td>Nrf2/HO-1 pathway</td>
<td>HO-1 enzyme regulates vascular function and NO production.</td>
<td>In diabetes, HO-1 gene expression and enzyme activity are reduced, leading to decreased cGMP levels in cavernous tissue. Inducers of HO-1 can indirectly enhance the effect of eNOS on the vasculature, affecting NO production.</td>
<td>[31]</td>
</tr>
<tr>
<td>Sirtuin 1 (SIRT1)</td>
<td>SIRT1 regulates eNOS activity, promotes NO production, and maintains vascular endothelial function.</td>
<td>In diabetes, SIRT1 function may be impaired, leading to reduced NO production, endothelial dysfunction, decreased vasodilatory activity, and accelerated endothelial cell senescence.</td>
<td>[32-34]</td>
</tr>
<tr>
<td>Tumor necrosis factor-α (TNF-α)</td>
<td>TNF-α is involved in immune responses and cellular signaling.</td>
<td>Elevated TNF-α levels in diabetes affect NO production by upregulating arginine expression and downregulating eNOS expression in endothelial cells, further impairing vascular function.</td>
<td>[35, 36]</td>
</tr>
<tr>
<td>Arginase</td>
<td>L-arginine is converted to NO by NOS, maintaining vasodilation and endothelial function.</td>
<td>Elevated ROS levels in diabetes interfere with NO production, reduce NO activity, and cause endothelial damage and vascular dysfunction.</td>
<td>[37, 38]</td>
</tr>
<tr>
<td>Oxidative stress</td>
<td>ROS and NADPH oxidase are involved in normal cellular metabolism and signaling.</td>
<td>Decreased superoxide dismutase (SOD) levels prevent effective ROS scavenging.</td>
<td>[39, 40]</td>
</tr>
<tr>
<td>Testosterone, T</td>
<td>T regulates NOS activity, induces NO synthesis, and participates in penile erection through the L-Arg-NO-cGMP pathway.</td>
<td>Decreased T levels in diabetes inhibit NO synthesis and activity, leading to inhibition of the NO-cGMP signaling pathway, reduced NO synthesis in the penis, and erectile dysfunction.</td>
<td>[41, 42]</td>
</tr>
<tr>
<td>Mitogen-activated protein kinase (MAPK) pathway</td>
<td>Involved in cell differentiation, proliferation, apoptosis, and regulation of various physiological processes.</td>
<td>Increased ERK1/2 levels in the corpus cavernosum of patients with diabetes mellitus inhibit eNOS activity. Activation of JNK and p38MAPK exacerbates fibrosis. MAPK pathway activation leads to endothelial dysfunction and penile cavernous fibrosis.</td>
<td>[43, 44]</td>
</tr>
<tr>
<td>RhoA/Rho kinase signaling pathway</td>
<td>Regulates cell proliferation, apoptosis, morphology maintenance, smooth muscle contraction, and other biological behaviors.</td>
<td>Activation of the RhoA/Rho kinase signaling pathway in diabetes leads to increased cavernous smooth muscle contraction, inhibition of eNOS activity, reduced NO production, and affects NO/cGMP pathway activity during erection.</td>
<td>[45, 46]</td>
</tr>
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</table>
medical therapy

Oral drugs: PDE-5 inhibitors are currently the first choice for the treatment of DMED, including sildenafil, vardenafil, tadalafl and avanafil, which have the advantages of good safety, high acceptability and few side effects. They can increase intracellular cGMP concentration and improve smooth muscle relaxation function by competitively inhibiting PDE-5 activity [47]. Several PDE5i have similar efficacy in the treatment of ED, but there are some differences in the time to peak blood concentration, half-life of blood concentration, and selectivity of PDE5 among different drugs [48, 49] (Table 3). Apomorphine, a dopamine receptor agonist, acts on dopamine D2-like receptors in the paraventricular nucleus and medial preoptic area of the hypothalamus, stimulating central dopaminergic collaterals to initiate erectile function, and clinical trials have also proved its efficacy in the treatment of DMED [50]. If the effect of PDE-5 inhibitor is not good, the patient's serum testosterone level should be considered. For patients with low serum testosterone levels, testosterone replacement therapy is effective [51], and testosterone can regulate the production of neurogenic NO and contribute to erection [22]. In addition, the combination of testosterone replacement therapy and PDE-5 inhibitors may have a more significant effect on the treatment of male erectile dysfunction (ED) patients [52].

Penile cavernous body vasoactive drug injection and urethral suppository treatment. In patients with ED who do not have a response to oral agents, intracavernous injection of vasoactive agents is a viable option. Common drugs include prostaglandin E1, papaverine, and phentolamine, all of which cause smooth muscle and vascular relaxation through different mechanisms of action for therapeutic purposes. However, this method has the risk of complications, such as penile pain, priapism, fibrosis of the corpus cavernosal body, and infection [53]. In order to improve efficacy and reduce adverse reactions, a combination strategy of PGE1 and papaverine or phentolamine is often used in clinical practice. In addition, there are also transurethral preparations of PGE1, which are less invasive and more convenient to use, although their efficacy is worse than that of injection. Alprostadil can also be administered by urethra, and can play a unique role in the urethral administration of alprostadil for DMED [54]. According to statistics, although the effective rate of cavernosal drug injection for DMED patients is up to 75%, the failure rate is also high within 2-3 months, up to 41-68% [55]. Therefore, efficacy needs to be weighed against potential risks when choosing a treatment.

Physical therapy

At present, there are two non-invasive physical therapy methods for DMED patients who do not respond well to oral PDE-5 inhibitors and cannot tolerate invasive treatment: vacuum compression device (VCD) and low-energy extracorporeal shock wave therapy (LI-ESWT). VCD achieves an artificial erection by applying negative pressure, attracting arterial blood to the penis, and limiting venous blood outflow. However, this method is inconvenient to use and may cause side effects such as cold penis, pain, and congestion. The spouse may also affect the success rate of VCD treatment [56]. VCD may also be related to increasing SO2 in the blood of the corpus cavernosum to resist hypoxia [57]. Low-intensity extracorporeal shock wave therapy (LI-ESWT) is mainly used to treat mild vasogenic ED. Although the specific efficacy of LI-ESWT in diabetic patients with ED remains to be further observed, studies have shown that LI-ESWT can significantly improve erectile function in patients with vasogenic ED [58].

Surgical treatment

The surgical treatment of DMED is mainly penile prosthesis implantation (PPI), which is suitable for patients with serious conditions who want to improve erectile function through surgery. Implants usually include three types: silicone, semi-rigid, and fluid-filled type. Silicone implants are the earliest type of penile prostheses, which can be used for a long time and have good tissue compatibility. Semi-rigid prostheses have better hardness and flexibility, and have short recovery time after surgery. However, they cannot completely mimic normal physiological structures. The fluid-filled type consists of a cylinder, a control pump, and a reservoir, and the thickness and hardness of the cylinder can be adjusted by an external pump. Surgery may be accompanied by complications, including intraoperative complications such as cavernosal body injury and urethral perforation [59], and postoperative complications such as mechanical failure, infection, and pain. Notably, the level of preoperative glycemic control was strongly associated with the incidence of postoperative pain and infection [60].

Exploration of new treatment techniques

With the deepening of the research on DMED, some new experimental treatment methods continue to appear. Stem cell therapy may be a promising treatment for erectile dysfunction by injecting various types of stem cells (such as autologous bone marrow mononuclear cells) derived from adipose tissue, bone, or human urine into the cavernous body to improve erectile dysfunction, some of which have achieved satisfactory results in clinical trials [61, 62]. The mechanism of stem cells in the treatment of diabetic erectile dysfunction may be related to promoting the recovery of cavernous microvascular smooth muscle and endothelial function, improving cavernous fibrosis, improving peripheral nerve and autonomic neuropathy in diabetic ED patients, and weakening cell ferropotosis [63-65]. However, research on stem cell therapy for human ED is still limited, and more studies are needed to prove its safety and efficacy [66].

The efficacy and safety of melanocortin receptor agonists have been evaluated in ED patients. In one study, subcutaneous injection of melanocortin II was effective in inducing an erection, but some patients experienced severe nausea and yawning [67]. Intranasal administration of Bremelanotide, another melanocortin receptor agonist, also significantly improves erectile function in diabetic ED patients or in those who have failed PDE5 inhibitors, but also causes nausea and hypotension [68]. Further clinical development of this class of agents has been limited by a lack of tolerability. Soluble guanylate cyclase activator can improve ED by increasing the level of cGMP [69]. Rho-kinase inhibitors can also improve the relaxation function of corpus cavernosal smooth muscle and reduce systemic fibrosis to improve ED [70]. In the rat experiment, clavulanic acid has shown significant potential to improve erectile function, especially

| Table 3 Comparative analysis of four commonly used PDE5 inhibitors |
|-------------------------------------|--------------------|-------------------|
| Time to reach peak blood concentration | Sildenafil | Tadalafil | Vardenafil | Avanafil |
| Half-life (h) | 3–5 | 15–17.5 | 4–5 | 5–17 |
| Effect of food on drug efficacy | Decreased Cmax, delayed Tmax | No effect | Decreased Cmax | Decreased Cmax, delayed Tmax |
| Selectivity for PDE5 | 10 times | 700 times | 15 times | 100 times |
| Cmax: Peak serum concentration, Tmax: Time to reach peak concentration |
after long-term treatment, which may be related to its role in the central nervous system [71]. Corpus cavernosum injection of calcium-sensitive Maxi-K ion channel gene (hSlo CDNA) can induce cavernous smooth muscle relaxation by opening intracellular potassium channels [72], but related studies have not been carried out further, possibly due to the safety and ethics of gene therapy. Traditional medicines have shown potential value in the treatment of diabetic erectile dysfunction. Eacmonae Cortex, widely used in traditional Chinese medicine prescriptions, has been found to improve the condition of DMED rats by ameliorating spinal cord nerve injury [73]. Yam Protein from Dioscorea polysachytra Turcz. It can reverse high glucose-induced endothelial cell damage in the corpus cavernosum of mice. Cordyceps militaris (CM), a fungal medicine, can increase superoxide dismutase activity, reduce malondialdehyde levels, and improve erectile function in rats by inhibiting oxidative stress and increasing NOS activity and testosterone levels [74]. Berberine, found in traditional Chinese medicines such as Huang Lian (Coptidis Rhizome), can improve oxidative stress in the corpus cavernosum and enhance the relaxation function of corpus cavernosum smooth muscle cells by inhibiting the expression and activity of tyrosine kinase 2 (JAK2) in DMED rats [75].

Summary

Modern medicine provides a variety of treatment methods for DMED, including oral drugs, cavernosal injection, physical therapy and even surgery. Although these approaches are able to relieve patients’ symptoms to some extent, there are significant limitations to their effectiveness and applicability. First, drug therapy, which is commonly used as an initial treatment, does not always work as expected. Some patients may seek other treatment methods because of adverse reactions or poor efficacy of drugs. However, these methods are inconvenient to use and have a high risk of complications. Second, although surgical treatment may be a viable option in some cases, it also carries the risk of complications and may place greater financial pressure on patients. In addition, it is worth noting that most of the current treatment methods mainly focus on ED, and there is still a lack of specific and effective treatment for DMED. Finally, although emerging therapeutic technologies have shown certain therapeutic potential in recent years, further research and clinical trials are still needed to verify their safety and efficacy before they are widely used in clinical practice. Therefore, the medical community still faces many challenges in the treatment of DMED, and there is an urgent need to develop more effective and safe therapeutic approaches.

References


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52. Jacob BC. Testosterone Replacement Therapy in Males With...


