

## SEXUAL MEDICINE REVIEWS

## Diabetes and Sexuality

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## ABSTRACT

**Introduction:** Deterioration in sexual functioning is one of the major and serious complications of diabetes. This common metabolic disorder not only affects sexuality through microvascular and nerve damage but also has psychological aspects. In men, the primary complications are erectile dysfunction, ejaculatory dysfunction, and loss of libido. Women similarly experience sexual problems, including decreased libido and painful intercourse.

**Aim:** To summarize the effects of diabetes on sexuality, evaluate the impact of diabetes on sexual function, and assess the conventional and novel treatment approaches based on recent studies.

**Methods:** A literature review of peer-reviewed journal articles and guidelines was performed.

**Main Outcome Measures:** To assess the effects of diabetes on sexuality and to focus on treatment approaches.

**Results:** Male and female sexual dysfunctions are a significant complication of diabetes. Tight glycemic control seems to be beneficial in delaying the onset of sexual problems and ameliorating them when they are present. Erectile dysfunction occurs as one of the first problems. The current mainstay of treatment for erectile dysfunction is therapy with phosphodiesterase type 5 inhibitors and then a stepwise approach of management. Men also can experience ejaculation problems and loss of libido. Diabetes also can decrease testosterone levels, which further decreases libido. Hypogonadal men with diabetes might benefit from testosterone replacement therapy. Diabetic women also can have sexual problems. These problems mainly include loss of libido, decrease in arousal and lubrication resulting in painful intercourse, and loss of orgasm. All these challenges require a multidisciplinary approach.

**Conclusion:** Diabetes has detrimental effects on the sexual function of patients. Diabetologists who primarily care for the patient should not only focus on the glycemic control of their patients but also address their sexual complaints, because these problems can significantly impair their quality of life. Urologists, gynecologists, endocrinologists, and psychiatrists should work in a multidisciplinary manner for the treatment of decreased sexual functioning as a result of diabetes.

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**Key Words:** Diabetes; Complications; Ejaculatory Disorder; Erectile Dysfunction; Quality of Life; Libido; Sexual Dysfunction; Testosterone

## INTRODUCTION

Diabetes mellitus (DM) is a common chronic disease that affects 0.5% to 2% of the world population.<sup>1</sup> DM and its treatments can lead to many complications. The main long-term complications are cardiovascular diseases (hypertension, heart failure, and atherosclerosis),<sup>2</sup> chronic renal disease (nephropathy),<sup>3</sup>

retinopathy,<sup>4</sup> and peripheral neuropathy.<sup>5,6</sup> DM causes these complications through vascular, neurogenic, and psychogenic pathways.<sup>7</sup>

DM also can lead to sexual problems in men and women.<sup>8</sup> Several epidemiologic studies have clearly demonstrated that DM is an important risk factor for erectile dysfunction (ED).<sup>9,10</sup> A threefold increased risk of ED has been reported in diabetic compared with non-diabetic men.<sup>10</sup> Men also can experience problems with ejaculation and libido,<sup>11</sup> whereas women can have problems with decreased sexual response and vaginal lubrication.<sup>12</sup> In diabetic women, this relation is less conclusive; however, several studies have reported a higher incidence of female sexual dysfunction compared with non-diabetic women.<sup>13,14</sup>

These complications occur mainly because of vascular and neuronal damage in patients with DM and glycemic control

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seems to be beneficial in the treatment and delaying the onset of these complications.<sup>15</sup> Hyperglycemia is the main determinant of pathogenic mechanisms related to sexual dysfunction in DM, although hypertension, obesity, metabolic syndrome, cigarette smoking, and atherogenic dyslipidemia can contribute to the development of sexual dysfunction in men and women.<sup>16–20</sup>

The aim of this review is to summarize the effects of DM on sexuality and assess the conventional and novel approaches for the treatment of sexual problems.

## ERECTILE DYSFUNCTION

ED is defined as the inability to achieve and maintain penile erection necessary for sexual intercourse.<sup>21</sup> ED is a prevalent condition in aging men and is frequently encountered in those with diabetes.<sup>22</sup> According to the Massachusetts Male Aging Study results, ED prevalence is threefold higher in diabetic compared with non-diabetic men and two times higher according to the age-dependent ED prevalence.<sup>23</sup> Moreover, ED occurs at a younger age in patients with DM, and it can develop 20 years sooner than in non-diabetics.<sup>24–26</sup>

### Pathogenesis of ED in Diabetes

The pathogenesis of ED in diabetic men is a multifactorial phenomenon in which vasculopathy, neuropathy, visceral adiposity, insulin resistance, and hypogonadism play roles.<sup>27</sup> Chronic hyperglycemia can result in endothelial dysfunction,<sup>28</sup> mainly because of the decreased bioavailability of nitric oxide, resulting in insufficient relaxation of the vascular smooth muscles of the corpora cavernosa. Impaired endothelial and neuronal nitric oxide synthesis leads to imbalance between the vasoconstrictor and vaso-relaxant pathways, favoring vasoconstriction.<sup>29,30</sup> Comorbidities, such as metabolic syndrome, hypertension, and smoking, can worsen erectile function in diabetic men.<sup>17,31,32</sup> Somatic and autonomic neuropathies also contribute to diabetic ED owing to decreased sensory impulses from the penis to the reflexogenic erectile center.<sup>33</sup>

Hormonal factors also play role in the development of ED in diabetic men. Testosterone concentrations tend to decrease in association with low levels of luteinizing hormone and follicle-stimulating hormone.<sup>34</sup> Testosterone is the hormone that affects sexual desire in men and women<sup>35</sup> and DM decreases libido by lowering testosterone levels.<sup>36</sup> Several studies have demonstrated a significant association between low testosterone levels and ED in men with DM.<sup>36,37</sup>

### Treatment of ED

Owing to its multifactorial etiology, diabetic ED necessitates a multidisciplinary approach. Appropriate glycemic control can decrease the risk of ED in diabetic men.<sup>15</sup> Tight glycemic control by maintaining glycosylated hemoglobin below 7% helps to minimize the risk of long-term microvascular complications of DM.<sup>38</sup> The Diabetes Control and Complications Trial<sup>39</sup> and the

United Kingdom Prospective Diabetes Study<sup>40</sup> found that intensive glycemic control was effective for the prevention of neuropathy, a condition that can impair sensory feedback from the penis leading to decreased erectile function.

However, glycemic control might not be sufficient for the treatment of ED in all diabetic patients. In a recent study, the effect of lifestyle modifications and glycemic control was compared with the efficiency of sildenafil citrate in 83 patients with type 2 DM and ED.<sup>41</sup> Group 1 (n = 41) received lifestyle modification (diet and exercise) and medical treatment for intensive glycemic control, whereas group 2 (n = 42) received sildenafil 100 mg for 2 to 3 weeks in addition to intensive glycemic control. The investigators reported more favorable erectile function outcomes in patients receiving sildenafil 100 mg after 3 months of treatment and concluded that only glycemic control and lifestyle changes are not adequate for better sexual function in diabetic patients with ED. Therefore, initiation of phosphodiesterase type 5 (PDE5) inhibitors as first-line therapy to men with DM who seek treatment for ED can result in significant improvement in erectile function and quality of life.<sup>42,43</sup>

Although all PDE5 inhibitors are equally effective in diabetic patients,<sup>44</sup> diabetics respond poorly to these agents compared with non-diabetic patients with ED.<sup>45</sup> Decreased nitric oxide activity and low testosterone levels in diabetic men might be responsible for this relatively low efficacy.<sup>45</sup> Long-term or daily use of PDE5 inhibitors might improve endothelial dysfunction in diabetics<sup>46</sup>; however, more controlled studies are required to confirm these findings. Men who do not respond to PDE5 inhibitors sufficiently or cannot use PDE5 inhibitors owing to contraindications should be referred to a specialist. These men might benefit from second-line therapies (eg, vacuum constriction devices, intracorporal injection therapy with prostaglandin E<sub>1</sub> alone or in combination with papaverine and phentolamine, or intraurethral therapy using alprostadil) or third-line therapy (penile prosthesis).<sup>47–49</sup>

Testosterone replacement therapy (TRT) is recommended for diabetic men whose testosterone levels are low.<sup>50</sup> Different testosterone therapies are available and the transdermal formulation has been shown to lessen ED in diabetic men in a prospective, randomized trial.<sup>51</sup> However, there are safety concerns regarding TRT, especially in the elderly population; therefore, hematologic, cardiovascular, breast, and prostatic assessments should be performed before the initiation of treatment.<sup>52</sup>

In addition to these therapeutic approaches, there are several currently available treatment alternatives. In a recent study, the effect of low-intensity pulsed ultrasound was investigated as a treatment for ED in a rat model of type 1 DM induced by streptozotocin (STZ). The study found that low-intensity pulsed ultrasound therapy improved erectile function and reversed pathologic changes in the penile tissue of rats with STZ-induced DM, indicating that low-intensity pulsed ultrasound therapy has the potential of becoming a non-invasive treatment alternative for diabetic ED.<sup>53</sup>

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