

## Review

# Sexual dysfunction in diabetic women

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## INTRODUCTION

Diabetes mellitus (DM) is a common disease worldwide and a growing public health burden. The number of people with diabetes is increasing due to population growth, aging, urbanization, and increasing prevalence of obesity and physical inactivity.<sup>1</sup> Diabetes is known to cause multiple medical,<sup>2</sup> psychological,<sup>3</sup> and sexual<sup>4</sup> dysfunctions. Increased prevalence of diabetes will inevitably result in increasing prevalence of its complications and their associated consequences.

Impaired sexual function in men is a well-documented complication of diabetes. The first mention of this disorder was made in the 10<sup>th</sup> century AD when the Persian physician and philosopher Avicenna described the “collapse of sexual functions” in men with diabetes.<sup>5</sup> Numerous presentday studies have shown that men with diabetes are indeed at increased risk for erectile dysfunction, which occurs at an earlier age<sup>6-10</sup> than in non-diabetics and is related to duration of diabetes, poor metabolic control, and the presence of diabetic complications.<sup>11</sup> Sexual dysfunction can be the first sign of the disease and also an indication of the patient’s vascular status.

In contrast, sexual problems of women with diabetes and associated risk factors are less clear and

have received less attention than those of men,<sup>12</sup> despite the fact that the risk for developing diabetic complications is the same in men and women with diabetes. Nevertheless, data on the sexual function of diabetic women have recently been published indicating that women with diabetes are also at increased risk for sexual dysfunction.<sup>4,13</sup> Discrepancies, however, still exist regarding the prevalence of female sexual dysfunction (FSD) in women with diabetes and the possible mechanisms implicated in its pathogenesis, although both organic and psychological factors seem to act synergistically.

This review aims to discuss diabetic FSD, while defining the parameters of dysfunction, and to present suggested risk factors and pathogenetic pathways as well as offer evidence-based strategies for the evaluation of sexual dysfunction and management.

## FEMALE SEXUAL DYSFUNCTION: DEFINITION, PREVALENCE, AND ETIOLOGIES

Female sexual function is complex and encompasses physical and emotional well-being across the lifespan. In general, studies of sexual dysfunction in women have lagged behind those in men due to several factors, the lack of standardized definitions of sexual dysfunction in women being one of them. Understanding the effect of diabetes on FSD presupposes knowledge of the various ways through which FSD has been defined and of the contribution of the ongoing changes to the conceptualization of sexual disorders.

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Masters and Johnson in the early 1950's<sup>14</sup> and Kaplan in the late 1970's<sup>15</sup> defined human sexual response based on studies of the physiology and psychology of human sexuality. They developed the linear sexual response model for men and women that consists of sequential stages of desire, arousal, orgasm, and resolution.<sup>16,17</sup> Thus, non-overlapping phases of sexual response have been described and according to this model discrete dysfunctions have been defined. However, over the past two decades research on women's sexual problems have resulted in expanded definitions of women's sexual dysfunctions due to the highly contextual nature of women's sexuality. These new definitions continue to reflect phases of sexual response, but they additionally clarify the tendency of the phases to overlap.<sup>16,18</sup> The newly defined models of female sexual response include physical, emotional, and cognitive feedback.<sup>19</sup> Over the last few years, evidence has emerged supporting the inclusion of "distress" in the definition of FSD;<sup>20</sup> however, the interpretation of the term "distress" can vary according to the woman's perception, from a persistent deterioration of the female psychology to a simple concern.<sup>5</sup>

Three classical medical definitions for FSD are generally accepted and have been provided by well recognized medical resources. The ICD-10 classification focuses on physical factors that influence sexual response,<sup>21</sup> the Diagnostic and Statistical Manual (DSM) – IV underlines the emotional and psychological factors involved in FSD,<sup>22</sup> and the most recent classification from the American Foundation of Urological Disease (AFUD) combines the previous classifications with the newest cyclic sexual response model proposed by Basson.<sup>23</sup> Newer and revised definitions of FSD by the American Psychiatric Association are expected to be published in their 2012 DSM – V.

Thus the prevalence rates of FSD differ in the various studies, depending on the criteria applied for its definition. Despite these uncertainties, sexual dysfunction in women seems to be more common than once thought. Large epidemiological studies of sexual attitudes and behaviours in men and women showed sexual difficulties to be common in middle-aged adults worldwide<sup>24</sup> and in women the reported rates to range between 40-60% in women.<sup>25-28</sup> Laumann et al<sup>25</sup> reported that 43% of women in the United States, aged

18 to 59 years, had sexual concerns. Dennerstein et al showed that FSD prevalence increased from 42% to 88% from the early to late menopause period.<sup>29</sup> The addition of sexual distress in the definition of FSD results in lower prevalence rates (9%) in the general population. Although data are scant and there is a great deal of uncertainty, lack of subjective arousal has been observed in 17% of women,<sup>30</sup> insufficient vaginal lubrication in 5-28%,<sup>25,30,31</sup> orgasmic disorder in 5%,<sup>32</sup> and dyspareunia (painful intercourse) in 3-12%.<sup>25,30-33</sup>

The etiology of women's sexual dysfunction is multifactorial and combines interpersonal, contextual (social), psychological, and biological factors.<sup>34</sup> In fact, every factor implicated in normal female sexual function can be a potential sexual dysfunction cause, while there is a strong association with psychological health issues<sup>25,35,36</sup> such as depression, anxiety, low self-esteem issues, body image perception disorders, fear of rejection, sexual performance anxiety, traumatic sexual experience in the past, and history of abuse. A second major factor is the quality of the relationship.<sup>35</sup> Only recently have biological risk factors received attention, including several medical conditions (urogenital, neurological, and endocrine disorders, pelvic floor disorders, menopause, pregnancy, obesity) as well as pharmacological and other therapies (anti-neoplastic agents, antipsychotic and antidepressant medications, antihypertensive agents, major surgical operations, radiation therapies).<sup>37</sup> Finally, limited social relations, financial difficulties, employment status, religious beliefs, educational background, and lack of exercise<sup>38</sup> comprise the sociocultural risk factors of FSD.<sup>39</sup>

## DIABETES MELLITUS AND FEMALE SEXUAL DYSFUNCTION

Despite the inconsistency that exists in the literature concerning this issue, it seems evident that the effect of diabetes on female sexuality is variable and could affect all the domains of sexual function. A mixed pattern of dysfunctional symptoms has commonly been reported, such as reduction or loss of sexual interest or desire, arousal or lubrication difficulties, dyspareunia, and loss of the ability to reach orgasm.<sup>13</sup> Studies in the literature conducted

in several ethnic groups (US, Italian, Polish, Turkish, Iranian, Jordanian, Nigerian, Peruvian populations) have reported a high prevalence of sexual dysfunction in women with either type 1 or type 2 diabetes.<sup>40-53</sup> These data are important since various cultures, religions, lifestyle habits and sexual behaviours are considered. Although the prevalence varies (Table 1)<sup>40,42-53</sup> depending on the criteria used to define sexual dysfunction in each study, it appears that sexual dysfunction is slightly lower in women compared to men,<sup>13,54,55</sup> it is twice that of the population without diabetes,<sup>13,40,45,48,56</sup> and it includes all the domains of sexual dysfunction. Whether desire is affected by diabetes remains controversial as some studies have

shown a 20-78% decrease in desire in women with diabetes (with the higher prevalence encountered in type 2 diabetes), while others have found no effect at all.<sup>43-45,47,51,52</sup> The incidence of arousal problems in women with diabetes is also variable, depending on the type of diabetes and the definition of arousal, and varies from 14 to 76% to no effect at all.<sup>42-47,49,51,52</sup> Regarding orgasm, most studies have indicated problems in women with diabetes ranging from 10-84%,<sup>43-46,49</sup> with a few studies showing no effect.<sup>56</sup> Finally, the risk of dyspareunia in women with diabetes varies from zero to 43%, with the higher prevalence being observed in type 2 diabetes.<sup>42,49,50</sup>

**Table 1.** Clinical studies on sexual dysfunction in women with diabetes

Author (year) Ref	Type of Diabetes Mellitus (DM)	Number of Diabetic women studied	FSD prevalence %	Sexual domains affected
Erol et al (2003) <sup>41</sup>	DM2	72	51.3	All
Enzlin et al (2003) <sup>40</sup>	DM1	97	27	Lubrication
Doruk et al (2005) <sup>46</sup>	DM1	18	71	Arousal, Lubrication, Orgasm
	DM2	25	42 (Non significant)	Arousal
Olarinoye et al (2008) <sup>42</sup>	DM2	51	Significantly higher FSD (Prevalence not reported)	Arousal, Orgasm, Pain, Satisfaction
Abu Ali et al (2008) <sup>43</sup>	DM1 - DM2	613	59.6 (Does not distinguish between the 2 types)	Desire, Arousal, Lubrication, Orgasm
Mezones-Helguin et al (2008) <sup>47</sup>	DM2	36	75	All
Fatemi et al (2009) <sup>44</sup>	DM2	50	Prevalence not reported	Desire, Arousal, Lubrication, Orgasm, Satisfaction (No pain domain in the study)
Enzlin (2009) <sup>48</sup>	DM1	424	35	No control group
Veronelli et al (2009) <sup>49</sup>	DM1	18	Prevalence not reported	Arousal, Lubrication, Orgasm, Pain
	DM2	10		
Wallner et al (2009) <sup>50</sup>	DM1	26	Prevalence not reported Does not show correlation between FSD and DM 1/2	Dyspareunia
	DM2	75		
Ogbera et al (2009) <sup>51</sup>	DM2	58	88 (Non significant)	Desire, Arousal, Satisfaction
Nowosielsky et al (2010) <sup>52</sup>	DM1	118	26.5	Desire, Arousal, Lubrication
	DM2	146	42.2	All
Esposito et al (2010) <sup>53</sup>	DM2	595	53	No control group

DM: diabetes mellitus; FSD: female sexual dysfunction.

## **PATHOGENESIS OF FEMALE SEXUAL DYSFUNCTION IN DIABETES**

The pathogenetic factors of sexual dysfunction among diabetic women include hyperglycaemia, infections, as well as vascular, neural, neurovascular and psychosocial derangements. However, pertinent data in the few published studies are conflicting.<sup>5,13,60,61</sup>

It has been hypothesized that hyperglycaemia, by reducing hydration of mucus membranes, including those in the vaginal tissue, results in poor vaginal lubrication and dyspareunia.<sup>62</sup> Also, hyperglycaemia may potentially lead to dyspareunia because of its association with an increased incidence of genitourinary infections. The symptoms of these infections (burning, itching, urgency, vaginal dryness or discharge, pain, general discomfort in the pelvic floor), the required treatment, the sexual abstinence recommended as part of some therapies, and the psychological distress involved could lead to vaginal discomfort and dyspareunia.

The normal female sexual response requires an intact sensory and autonomic nervous system to ensure proper interpretation of and response to erotic stimuli. Sexual arousal largely depends on the sympathetic nervous system. Moreover, nonadrenergic/noncholinergic neurotransmitters (NANC), e.g. vasoactive intestinal polypeptide (VIP) and nitric oxide (NO), are involved in smooth muscle relaxation and enhancement of genital blood flow and thus may influence sexual function. Diabetes causes vascular and nerve dysfunction which can lead to structural and functional changes in female genitalia and may impair sexual response. Over the past two decades, advances have been made in exploring the basic hemodynamics and neuroregulation of female sexual function and dysfunction in both animal models and human studies. Studies in animals have indicated that diabetes, by inducing structural and functional changes in the female genital tract, may result in impaired arousal and orgasmic sexual response.<sup>63,64</sup> In a rat model of streptozotocin-induced diabetes it has been shown that diabetes impaired the relaxation responses of the vaginal tissue to almost all transmitter systems [i.e. to electrical stimulation of nerves (EFS), to NO donors, and to calcitonin gene-related peptide (CGRP)] and the contractile response of vaginal tissue to norepi-

nephine and to EFS.<sup>65</sup> Other rat studies have indicated that diabetes causes a significant decrease in nerve-stimulated clitoral and vaginal blood flow, induces diffuse fibrosis of the clitoris and the vaginal tissue, and reduces muscular layer and epithelial thickness in the vagina,<sup>63,64,66</sup> thus impairing sexual response. Studies in humans, using vaginal plethysmography as an objective measure of physiological arousal, have found an association between diabetes and decreased vaginal lubrication.<sup>48,67</sup> Moreover, in diabetic women a reduced vibration sense in their genitalia has been observed, but whether this symptom is related to sexual problems needs to be clarified.<sup>60</sup> Vascular changes or damage due to diabetes may lead to changes in the local blood flow and inhibition of the engorgement of the clitoris and lubrication of the vagina during arousal, resulting in dyspareunia or decreased arousal during sexual activity.<sup>63,66</sup> Additionally, the presence of diabetic neuropathy can have detrimental effects on the normal transduction of sexual stimuli as well as on the triggered sexual response<sup>61,68</sup> and may cause changes to the vaginal wall and pelvic floor dysfunction as a result of the weakened muscular tone. Arousal, orgasmic, and sexual pain disorders comprise the main consequences of the diabetic neuropathy.

Within the central nervous system, hypothalamic, limbic-hippocampal structures play a central role in sexual arousal. Furthermore, various hormones such as estrogens, testosterone, and progesterone may influence female sexual function. Estrogens play a significant role in maintaining the mucosal epithelium, the sensory thresholds, and the genital blood flow, and thus are important for desire.<sup>37</sup> Androgens primarily affect sexual desire, arousal, and orgasm and the overall sense of well-being, while progesterone seems to play a role in enhancing receptivity.<sup>37</sup> It has been suggested that androgen glucuronides, the metabolic derivatives of testosterone and dehydrotestosterone, can be used as a marker for assessing androgenic activity in women. Moreover, recent data have shown that compared to testosterone or dehydrotestosterone, the glucuronides could identify cases of true androgen deficiency that might be related to sexual dysfunction and possibly require androgen therapy.<sup>69</sup> Hormonal imbalance that accompanies DM has been hypothesized to play a potential role in the pathogenesis of the FSD. Epidemiological studies

conducted in female diabetic populations have shown a correlation between the observed changes in the levels of androgens, oestrogens, and sex hormone binding globulin (SHBG) and the desire and arousal problems in these women.<sup>70</sup> Additionally, several other endocrinopathies that may accompany diabetes, such as thyroid disorders, hypothalamic-pituitary disorders, and polycystic ovary syndrome, can contribute to sexual problems in these women.<sup>12</sup> In a recent study, decreased sexual function and increased sexual distress was observed during the luteal phase of the menstrual cycle in women with type 1 diabetes. In this study the decreased sexual function during the luteal phase was independent of mood deflections and glycaemic control.<sup>71</sup> More studies are obviously needed to define the effect of the various phases of the menstrual cycle on sexual function.

Depression seems to be the most established risk factor for sexual dysfunction in women with diabetes, especially considering that this cohort is at a high risk of developing depression.<sup>72</sup> Several studies have demonstrated that in women with diabetes, sexual dysfunction is predominantly linked to psychological factors.<sup>40,47,48,62,73,74</sup> Studies have also revealed that diabetic women with sexual dysfunction presented twice as many depressive symptoms as those without sexual dysfunction. In these women depression was related not only to decreased desire but also to arousal dysfunction.<sup>40</sup> However, there are no data as to whether the sexual problems disappear when depression is treated in women with diabetes. Furthermore, diabetes and its complications can harm the woman's self-image and self-confidence, her health and relationship status, her social life and daily routine, all of which could affect her sexual performance.<sup>75</sup>

Thus, in general, sexual dysfunction in women with diabetes appears to be quite complex, involving neurological, vascular, hormonal, and psychosocial aspects. Specific risk factors, however, including those related to DM, are difficult to identify. In contrast to studies in men, studies in diabetic women have indicated poor or no association between sexual problems and diabetes related parameters, such as cardiovascular, metabolic (i.e. glycemic control, diabetes duration) or other factors (i.e. age, BMI, menopause, use of hormone replacement therapy),<sup>40-42,46-48,56,58,62,74-76</sup> and have shown that their sexual response is more likely

affected by psychosocial aspects (e.g. depression).<sup>45,48,77</sup> Several factors account for the differences in sex risk factor profiles in men and women. Differences in the underlying pathophysiological mechanisms, such as differences in neurotransmitter involvement of sexual response in men and women,<sup>78,79</sup> might be implicated. Furthermore, although it is easy to quantify men's physiological sexual response by their erection, it is much more difficult for many women to recognise and appraise genital arousal and congestion.<sup>5,77,78,80-83</sup> Additionally, cultural and psychosocial factors seem to play a significant role in female sexuality, while depression is a more prevalent and potentially more powerful factor in women as compared to men.<sup>84</sup>

In general, the available data are controversial and the precise etiology and pathogenetic pathways of diabetes related female sexual disorders have not as yet been determined. Studies of sexual dysfunction in women with diabetes are few and have significant methodological drawbacks in that they include small sample sizes, lack standardized definitions of sexual dysfunction and well-validated scales and, finally, are inadequate in their characterization of diabetes, particularly with regard to type and glycemic control, existence of complications, psychological adjustment to diabetes, and presence or absence of depression.<sup>13,84,85</sup> Additionally, variation and differences in sexual dysfunction have been found between the two types of diabetes, although many studies have made no distinction between the two types. Women with type 2 diabetes seem to face more sexual problems in comparison to those with type 1. Older age, age-related factors such as menopause, chronic disease, higher degree of complications, and higher depression rates reported in women with type 2 diabetes may account for these differences.<sup>4,62,75,86,87</sup> Moreover, most studies make no distinction between pre- and post-menopausal women, while others exclude women with no relationship. In fact, women with no current sexual relationship might be those with the most severe sexual problems and distress that force them to avoid long-term relationships.

## DIAGNOSTIC APPROACH TO DIABETIC FEMALES WITH SEXUAL DYSFUNCTION

Assessing a woman's sexual function and its dis-

orders can be very challenging. A free talk about her sexual life and its problems may develop into an uncomfortable discussion for both the doctor and the patient. Personal taboos regarding sex, confidentiality issues, worries about potential humiliation, time constraints, even the doctor's limited experience in handling sexual problems, are a few of the factors that can impede the uncovering of possible sexual difficulties or disorders. Moreover, since many of the causes of FSD do not have a strict medical origin, one has to be careful when characterizing all woman's sexual problems as organic, as this can lead to mistaken diagnoses and further complicate their management.

To identify whether a diabetic woman has sexual dysfunction and prescribe appropriate treatment, factors that contribute to sexual dysfunction, such as the woman's current interpersonal and psychosocial status, her sexual and medical history, comorbid illness as well as her medication should be examined.<sup>31,88</sup> Sexual dysfunction can be a symptom of an underlying disorder or have causes outside the patient herself. To begin with, a thorough general medical history is essential. The physician should be aware not only of the duration of diabetes, the glycemic control, the presence or absence of chronic diabetic complications, the pharmacological treatment of diabetes but mainly the mood of the diabetic woman as this is the key to the whole process of her sexual enjoyment.<sup>67</sup> Even minor episodes of depression can affect the woman's sexual desire. Poor diabetic control or diabetic complications may cause depression and thus sexual dysfunction in women with diabetes. Hypoglycemia can also impair sexual function in a diabetic woman, as arousal, foreplay, intercourse, and orgasm are all activities of energy expenditure. Comorbid factors, history of surgical operations, medication use, menopausal status, personal habits such as smoking, alcohol intake, and type of exercise can provide useful information on the possible risk factors. During the general systems enquiry, questions about sexual function can follow the gynecological history. If a woman acknowledges sexual problems, a detailed interview of her and her partner both individually and together is usually necessary. The age of initiation of sexual activity, enquiries about sexual abuse or other traumatic sexual experiences, number of sexual partners, impact of religious and

social beliefs on sexuality should be taken into account. Moreover, information about the couple's current sexual life, practices, and complaints along with the degree of satisfaction that results from the sexual activity should be obtained.

In order to facilitate medical practice in the field of sexual medicine, several tools that estimate female sexual function have been developed. To assist physicians in the initial approach and evaluation of sexual function, two simple models have been proposed, namely ALLOW and PLISSIT (Table 2).<sup>37,89</sup> For a more detailed and extensive evaluation, structured interviews and self-reported validated questionnaires are the most commonly used methods. Structured interviews have a more personal character as they provide the opportunity for clarifying possible details, answering questions, and explaining terms; moreover, the physician has the chance to evaluate the patient's reactions during the interview. Validated questionnaires on the other hand are characterized by privacy and confidentiality, are adjusted to the female population, and can include measurable data that can be further analyzed.<sup>90</sup> The Female Sexual Function Index (FSFI), the Brief Index of Sexual Functioning for Women (BISF-W), the Derogatis Interview for Sexual Function (DISF/DISF – SR) and the Female Sexual Distress Scale (FSDS) are some of the available questionnaires that evaluate female sexual function and its disorders.<sup>91</sup> Nevertheless, because of the complexity of the female sexual function, resistant cases of FSD require a multidisciplinary approach, preferably conducted by appropriately trained physicians and specialists.<sup>92</sup>

**Table 2.** Available models for evaluating sexual function

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**The ALLOW model**

- Ask about sexual life
- Legitimize sexual problems
- Set limitations regarding sexual medicine practice
- Open up the discussion
- Work together to treat

**The PLISSIT model**

- Permission to discuss sexual problems
  - Provide limited information regarding sexuality
  - Provide specific suggestions on the reported problems
  - Refer for intensive treatment by a specialist
-

## THERAPEUTIC APPROACH TO SEXUAL DYSFUNCTION IN WOMEN WITH DIABETES

There are no specific guidelines for the treatment of FSD in diabetic women. Due to the large number of factors that can lead to sexual dysfunction in women with diabetes, effective treatment may entail psychological as well as pharmacological treatment, both applied by trained clinicians. Pharmacotherapy alone without addressing psychosocial issues has been proven to be unsuccessful.<sup>93</sup> In general, FSD that is identified early in the sexual response cycle and/or with long duration becomes more resistant to treatment. This means that the orgasmic disorder is easier to handle as compared with arousal or desire dysfunctions.<sup>94</sup>

Psychological issues, such as previous sexual education and experiences, relationship issues, anxiety and depression, and the mechanisms the patient has developed to cope with diabetes and life in general (seeking medical help, social or spiritual support, friendship, relaxing, pragmatism, anger, aversion) should be addressed. Cognitive-behavioral psychotherapy is the proposed treatment for women suffering from desire disorders or vaginismus, while couple therapy has been proven to result in greater partner intimacy.<sup>37,95</sup> Women with arousal or orgasm disorders can benefit from the FDA approved Eros clitoral therapy device.<sup>37,96-100</sup> The device is placed over the clitoris and creates a gentle vacuum that increases the genital blood flow, enhancing the genital sensitivity. The InterStim system is a nerve stimulation method originally intended as treatment for urine incontinence; it is now being tested for arousal disorders without, however, definite results.<sup>101</sup>

Treatment of depression is crucial for the diabetic women with sexual dysfunction, while appropriate and specific antidepressive medications are beneficial.<sup>37</sup> Frequently, since improvement of the glycaemic control tends to improve depressive symptoms, antidepressive medications can be discontinued.<sup>102</sup> Adequate glycaemic control is of paramount importance for the treatment of sexual dysfunction of diabetic women, who are encouraged to follow their antidiabetic treatment in order to ensure good glycaemic control and avoid complications. Furthermore, lifestyle changes such as implementation of a healthy and balanced

diet, regular exercise, and body weight control are suggested not only for achieving better glucose levels but because they have been found to improve female sexual function.<sup>95</sup>

Pharmacological treatment for FSD is also available and current treatment options are based on hormonal therapies and agents that act either centrally or peripherally. However, further research is needed in this domain for design of improved treatments. The choice of the appropriate medication depends on the type of sexual dysfunction.

The finding that hormonal replacement therapy improves sexual function parameters of menopausal women has led to the use of estrogens for the treatment of FSD, in general. Estrogens may improve sexual function by inducing the proliferation of the superficial cell layer of the vaginal mucosa, improving the vaginal pH and elasticity, and increasing vaginal blood flow to enhance lubrication.<sup>103</sup> However, when estrogens are used, the risks of such therapy should be taken into consideration, while careful choice of the most appropriate agent and route of administration are of major importance.<sup>95,103,104</sup> Importantly, in women with diabetes the effects of estrogens on lipid profile should be taken seriously into account.<sup>105</sup> Studies have established the role of testosterone in female sexual desire, arousal, genital sensation, and orgasm. Thus, finding that FSD is related to androgens deficiency should result in the systematic or topical use of testosterone for its management.<sup>106</sup> Testosterone seems to improve desire, arousal, and orgasm; however, due to its side effects, such as masculinization as well as adverse hepatic and cardiovascular effects, the long-term use for the treatment of the FSD is not recommended and further research is needed to establish its action and safety.<sup>103,106</sup>

Several other pharmaceutical therapies have been suggested. Tibolone has androgenic, estrogenic, and progesterone activity and it has been shown to improve desire, arousal, and lubrication.<sup>95,103,107</sup> Phentolamine is an  $\alpha$ -antagonist that improves arousal and lubrication;<sup>108</sup> apomorphine,<sup>94</sup>  $\alpha$ -melanocyte-stimulating hormones,<sup>109</sup> serotonin receptor antagonists,<sup>110</sup> and selective estrogen and androgen receptor modulators are in phase II trials.<sup>112</sup> Vasodilators as L-arginin,<sup>112</sup> alprostadil,<sup>113</sup> and herbal therapy (gingko biloba)<sup>112</sup>

have an as yet undetermined role in the treatment of FSD.

Phosphodiesterase type 5 inhibitors block the degradative action of type 5 phosphodiesterase on the cyclic GMP (second messenger in the NO mediated smooth muscle relaxation) and amplify vasodilatation.<sup>104</sup> Theoretically, they can assist the vaginal and clitoral vasodilation, improving vaginal lubrication and vulvar engorgement. Sildenafil use has had ambiguous results,<sup>114</sup> while the role of vardenafil and tadalafil in the treatment of FSD is still to be determined.<sup>104</sup> It has been proposed that the low levels of type 5 phosphodiesterase in the female reproductive system could account for these findings.<sup>115</sup>

## CONCLUSIONS

DM seems to impair women's normal sexual functioning. Recent evidence indicates that diabetic women are at higher risk for developing sexual dysfunction compared to those without diabetes. Type 2 diabetes seems to have a greater negative impact on female sexuality than type 1. It nevertheless remains unclear which domain of the sexual cycle is most affected in women with diabetes, the precise mechanisms via which diabetes adversely affects sexual function, and the importance of diabetes-related risk factors on the pathogenesis of FSD. However, current evidence indicates that psychosocial rather than organic factors are implicated in the pathogenesis of the sexual dysfunction in women with diabetes. Physicians should be aware of the problem and address issues of sexuality when they examine women with diabetes. They should be trained to use appropriate methodology for evaluating women's sexual function in order to identify pertinent pathology and refer them for the appropriate therapeutic approach. Thus, treatment for sexual dysfunctions of diabetic women includes lifestyle changes, optimal diabetic control, psychotherapy, and appropriately selected pharmacotherapy. Further research is obviously necessary to investigate the effects of the different types of diabetes on female sexuality so as to provide effective management options for these women.

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