

REVIEW

A Practical Approach to Managing Hypoactive Sexual Desire Disorder in Women with Diabetes

Charmaine Rochester-Eyeguokan · Lisa Meade

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ABSTRACT

Female sexual dysfunction (FSD) is highly prevalent in women with diabetes mellitus (DM), yet it remains unaddressed, undiagnosed, and untreated. Hypoactive sexual desire disorder (HSDD) is the most common complaint among women with FSD, but there is a paucity of research into its multifactorial etiology. Flibanserin is the only therapy approved by the US Food and Drug Administration for treating acquired, generalized HSDD in premenopausal women. Women with DM diagnosed with HSDD may require a multidisciplinary approach for optimal management.

Keywords: Diabetes mellitus (DM); Female sexual disorder (FSD); Flibanserin; Hypoactive sexual desire disorder (HSDD); Testosterone

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C. Rochester-Eyeguokan (✉)
Department of Pharmacy Practice and Science,
University of Maryland School of Pharmacy,
Baltimore, MD, USA
e-mail: lmeade@wingate.edu

L. Meade
Department of Pharmacy Practice, Wingate
University School of Pharmacy, Wingate, NC, USA

INTRODUCTION

Female sexual dysfunction (FSD) is highly prevalent in women with diabetes mellitus (DM) and affects their overall quality of life [1]. One large study reported an FSD prevalence in 35% of sexually active women with type 1 diabetes mellitus (T1DM) while another study reported a prevalence of 71% in T1DM, 42% in type 2 diabetes mellitus (T2DM), and 37% in a control group [1, 2].

In contrast to men with DM who have sexual dysfunction (SD), researchers found no association between women with DM who have FSD and cardiovascular risks factors, diabetes complications, HbA1c, menopausal status, glycemic control, diabetes duration, age, body mass index (BMI), the use of hormone replacement, or other medication therapies [1, 3]. Depression and marital status were the major predictors of FSD risk in women with DM [3].

FSD includes female arousal disorder (FAD), female orgasmic disorder (FOD), sexual pain disorder (SPD), and hypoactive sexual desire disorder (HSDD) [4]. HSDD is the most common complaint among women with SD, affecting approximately one in every ten women in the USA [5]. The absence of sexual fantasies and desire for sexual activity characterizes HSDD, causing significant personal distress or interpersonal difficulties [4]. Acquired HSDD develops in a patient who describes no previous sexual desire problems while generalized HSDD occurs irrespective of the type of sexual activity,

situation, or partner. Women with HSDD experience impaired body image, self-confidence, self-worth, frustration, grief, incompetence, loss, sadness, sorrow, or worry [6].

This article focuses on HSDD's pathophysiology, clinical presentation, and management, aiming to provide a practical approach to an under-recognized complication in women with DM. This article is based on previously conducted studies and does not involve any new studies of human or animal subjects performed by any of the authors.

PATHOPHYSIOLOGY

Normal Female Sexual Physiology

Normal sexual functioning in women consists of desire, arousal, plateau, orgasm, and resolution requiring a woman's sensory and automatic nervous system to respond to erotic stimuli [5]. Numerous neuromuscular and vasocongestive actions occur to increase desire and excitement by increasing clitoral diameter and length, vaginal lubrication, and wall engorgement. The smooth muscle relaxation of the female genital erectile tissue and increase in blood supply are dependent on the healthy action of neurotransmitters, primarily dopamine (DA) [5]. Key areas of the brain regulate sexual desire, while neurotransmitters such as DA, melanocortin, oxytocin, vasopressin, and norepinephrine coordinate pathways to process and respond to sexual stimuli [5]. Sex hormones, estradiol and testosterone, also increase sexual stimuli and sexual desire by facilitating DA release and enhancing nitric oxide synthesis. Nitric oxide regulates the blood supply and clitoral erectile function in females [5]. Sexual responses are integrated and dependent on the quality of the woman's interpersonal relationships, life stressors, finances, periods of abstinence, and her biologic and psychologic factors [7].

Sexual Dysfunction in Women with Diabetes Mellitus

Women with DM have additional pathophysiologic dysfunctions that increase their risk

above women without DM. Atherosclerosis, diabetic neuropathy, and diabetes-induced endothelial dysfunction, which occur in DM, cause FSD [5, 8]. Atherosclerosis reduces arterial blood supplying the female pelvic anatomy, inhibiting sexual response to stimuli by decreasing vaginal and clitoral engorgement, vaginal lubrication, sexual arousal, and nerve stimulation [5]. Prolonged hyperglycemia results in decreased mucus and vaginal lubrication and increased incidences of fungal and genitourinary infections [5].

Ovariectomy, menopause, polycystic ovarian syndrome, chemotherapy, gonadotropin-releasing hormone agonist, spironolactone, corticosteroid therapies, or adrenal insufficiency can cause testosterone deficiencies [8]. Because testosterone is vital for sexual stimuli and desire, having deficiencies can result in decreased vaginal lubrication and blood flow, inhibiting sexual response to stimuli causing dyspareunia, dysphoric mood, persistent fatigue, diminished desire, decreased sexual pleasure, or a lack of sexual receptivity [5, 8].

Hormonal imbalances accompanying DM such as thyroid and/or hypothalamic–pituitary disorders can cause loss of sexual desire, decreased vaginal lubrication, lack of orgasm, and increased coital pain [5, 8]. Poor body image and a fear of hypoglycemia during or after sexual activity increase anxiety and distress in women with DM [5]. In addition, psychosocial variables also affect a woman's desires such as feelings of guilt, embarrassment, and dissatisfaction related to DM [5].

There are also psychosocial variables that affect a woman's desire, including her relationship with her sexual partner, aging, menopausal status, comorbidities, and medications [5]. Additional factors thought to play a role in the pathogenesis of FSD include chronic conditions like rheumatoid disease, chronic pain, spinal cord injury, endometriosis, incontinence, depression, and hypertension [9]. Depression is associated with low sexual desire, low self-esteem, difficulty in experiencing pleasure, social problems, irritability leading to difficulties in maintaining relationships, and a lack of energy [5, 9].

Drugs can inhibit sexual desire and orgasmic experiences by decreasing brain DA levels, augmenting the action of brain serotonin, or increasing opioids at mu receptors, which can result in primary aversion or secondary avoidance behaviors [5]. Antipsychotics, neuroleptics, and antidepressants adversely affect arousal, desire, and orgasm [9]. Selective serotonin reuptake inhibitors (SSRIs) have a dose-related effect of increasing prolactin levels, thus reducing sexual desire and inhibiting orgasm [10]. Oral, but not transdermal estrogens, increase sex hormone binding globulin, which binds circulating testosterone and impairs the effect of testosterone [10].

HSDD is therefore an imbalance in sexual excitatory and inhibitory pathways, but other contributing factors such as psychological conditions, relationships, medical conditions, medications, and menopause increase the distress.

CLINICAL PRESENTATION/ DIAGNOSIS

Initiating the Conversation

A survey found that 72% of women want to speak with their health care professional about their sexual concerns, but 73% preferred if the health care provider initiated the conversation [7]. Because providers may lack training and knowledge to identify sexual issues, many women are reluctant to discuss their sexual problems with them [6]. The PLISSIT model (Permission, Limited Information, Specific Suggestions, and Intensive Therapy) is a helpful tool for clinicians to discuss sexual health or concerns with female patients. The tool provides the following guidance.

Permission

Clinicians should ask open-ended questions during routine history to give the patient the permission to discuss sexual concerns and reassure the patient that her feelings are normal. The clinician should allow the patient to discuss whether they were satisfied with their

current sexual relations, or what distresses them about their sexual problems [10]. When discussing sexual concerns with a patient, clinicians should use an open body posture, eye contact, avoiding nervous gestures, and carefully choose language appropriate to the patient's age and culture that will make the patient comfortable [10]. See Table 1.

Limited Information

The clinician should provide limited information regarding education on the female pelvic anatomy, sexual response cycle, etiology of sexual problems, and lifecycle changes in sexual function. Clinicians can also clarify that sexual interest or desire may not be the first response to stimuli, or that women may not always experience orgasm. Then the clinician should encourage sexual health follow-up appointments [7].

Table 1 Tips to facilitate dialogue [7, 10]

Tips to facilitate dialogue	
Posture and language	
Ask open-ended questions with silences that encourage the patient to speak	
Use words and body language that put the patient at ease	
Maintain an open, non-defensive body posture	
Sit and maintain eye contact	
Avoid nervous gestures	
Choose language appropriate to the age, ethnicity, and culture of the patient	
Questions	
Do you have any sexual concerns you would like to discuss?	
Are you satisfied with your current sexual relations?	
Please describe your sexual problem	
What distresses you the most about this sexual problem?	
“Tell me about [it]” are probably the four most powerful words in medicine	

Specific Suggestions

The clinician can suggest that women use specific therapy such as lubricants, over the counter moisturizers, or topical estrogen for vaginal dryness/dyspareunia. They should suggest planned date nights and teach patients to make sexual behavior a priority. Clinicians should encourage improved diet, exercise, and sleep patterns to help overall mood.

Intensive Therapy

The clinician can refer women for intensive therapy with a qualified sexual specialist or mental health specialist if the sexual concern exceeds their level of comfort or expertise. Women with diabetes and HSDD would benefit from a multidisciplinary team. Therefore, clinicians should be familiar with certified sexual therapists and counselors in the local area. The therapist should address psychosocial issues, including current and past abuse, current values, beliefs, and desires, and the health and well-being of the partner [7].

Diagnosis and Screening Tools for HSDD

As a result of the complexity of HSDD, it is difficult to diagnose. Symptoms include a decrease or absence of sexual desire for at least 6 months, which also causes personal distress. A detailed medical history including onset, duration, severity, and level of distress can help determine if the decrease in sexual desire is hormonal, neurological, metabolic, vascular, psychological, or some combination [6]. Complete loss of sexual desire is not required for diagnosis but only a change in desire for at least 3 months [6]. It is important to realize that overlapping sexual disorders are common; therefore, the clinician should ask about other sexual dysfunction in the female patient with HSDD [7]. The clinician should discuss which problem presented first and, in collaboration with the patient, address the primary disorder first [7].

A thorough sexual history should assess medical, reproductive (obstetric/gynecologic), surgical, psychiatric, social, and sexual information [6]. Providers should assess glycemic

control as well as thyroid hormone and prolactin levels to rule out any endocrine problem. Testosterone and estradiol levels can neither predict nor confirm HSDD [6]. In addition, clinicians should complete a thorough medication review for all patients to rule out medication-related risks of FSD. For example, clinicians should avoid prescribing SSRIs for women with HSDD.

The clinician can utilize a variety of validated screening instruments to assess HSDD. The decreased sexual desire screener (DSDS) is a validated, five-question tool completed by the patient to assess for generalized acquired HSDD [11]. The DSDS contains four “yes/no” questions, which assess the loss of sexual desire or distress. The clinician should diagnose HSDD if the woman answers the first four questions as “yes”. The fifth question can help make the differential diagnosis by identifying specific factors that may be contributing to the decrease in desire (medical conditions, medications, drugs or alcohol, menopausal symptoms, recent childbirth, pain with intercourse, decreased arousal or orgasm, partner’s sexual problems, relationship problems, stress, or fatigue) [11]. Table 2 lists evaluation strategies incorporating the screening tools and other factors in the patient’s assessment of HSDD.

Other screening tools include the female sexual function index (FSFI), which evaluates sexual satisfaction; the female sexual distress scale-revised (FSDS-R), which evaluates sexual distress; and the sexual interest and desire inventory-female (SIDI-F), which determines the severity of HSDD. Both the brief HSDD screener and the brief profile of female sexual function (B-PFSF) evaluate HSDD in postmenopausal women [7].

MANAGEMENT

The major goal of therapy is to restore sexual desire, which comprises of drive, cognitive, and motivation. Spontaneous sexual interest demonstrates drive, while cognitive incorporates sexual beliefs and values, and motivation demonstrates the willingness to participate in sexual activity [7]. Treatment options will differ

Table 2 Evaluation for HSDD [7, 11]

Step 1: Initiate the conversation using the PLISSIT model

Step 2: Utilize the screening tool: decreased sexual desire screener
An answer of “yes” to the first four questions is consistent with HSDD
Question 5 can identify reasons for the decrease in sexual desire

Step 3: Take a thorough sexual history considering psychosocial issues

- Relationship status
- History of abuse (verbal, emotional, physical, or sexual)
- Alcohol, tobacco, or illicit drug abuse

Step 4: Take a thorough sexual history considering medical/medication issues

- Current health status
- Past medical history
- Reproductive history and current status (age of menarche, menstrual history, obstetric history, infertility, contraception, sexually transmitted diseases, gynecologic problems, surgeries, urologic problems)
- Endocrine system (diabetes, thyroid disorders, hyperprolactinemia, androgen deficiency)
- Neurologic disorders
- Hypertension
- Psychiatric Illness (mood disorders, anxiety disorders, psychotic illness)
- Surgical history
- Medications (antidepressants, mood stabilizers, anticonvulsants, anticholinergics, opioids, amphetamines, hormones (estrogens, progestins), anti-androgens, GnRH agonists, antihypertensive agents (beta blockers, alpha blockers, diuretics), cardiovascular agents (triglyceride-lowering agents, digoxin), weight loss agents, histamine receptor blockers, chemotherapy agents, aromatase inhibitors, immunosuppressant therapies, steroids)
- Other chronic conditions (breast cancer, rheumatoid arthritis, psoriasis)

Step 5: Additional evaluation if needed

- Physical exam
- Gynecological examination
- Glycemic control
- Thyroid hormones
- Prolactin levels
- Testosterone and sex hormone binding globulin levels

Step 6. Refer to specialists if needed

- Certified sexual therapists
- Certified sexual counselors
- Psychiatrists or psychologists

HSDD hypoactive sexual desire disorder, *PLISSIT* permission limited information specific suggestions intensive therapy

depending on which component of desire the clinician deems compromised. For example, some women with cognitive dysfunction will benefit from cognitive behavior therapy or couples sex therapy, which focuses on changing thoughts, feelings, and behaviors [6]. Another woman may benefit from hormonal replacement therapy or centrally acting therapy to improve sexual functioning, still another may

benefit from psychotherapy when the clinician identifies psychological or interpersonal problems.

Because other comorbid conditions can affect sexual functioning, underlying factors such as depression, anxiety, incontinence, DM, hypertension, and cardiovascular disease must be treated and controlled.

Pharmacotherapy

Clinicians should recommend vaginal lubricants and moisturizers for vaginal dryness in women with DM who are postmenopausal or those with hyperglycemia, who complain of vaginal dryness or dyspareunia.

Flibanserin, a serotonin 1A receptor agonist and a serotonin 2A receptor antagonist, is the only US Food and Drug Administration (FDA)-approved agent for generalized acquired HSDD in premenopausal women [12]. The FDA approved flibanserin 100 mg with a risk evaluation and mitigation strategy (REMS) because of the increased risk of severe hypotension and syncope due to its interaction with alcohol. The REMS program certifies prescribers and pharmacists, who must counsel patients about this increased risk and interaction during flibanserin treatment. To reduce the risk of hypotension, sedation, and syncope, patients should take flibanserin before bedtime [12].

Flibanserin is not efficacious in patients with HSDD caused by medications, psychiatric problems, chronic disease, substance abuse, or relationship problems. Unlike sildenafil, flibanserin is not an on-demand medication, and it does not enhance sexual performance [12].

Three clinical trials evaluating the efficacy of flibanserin 100 mg in premenopausal women with acquired, generalized HSDD, demonstrated that about 10% more flibanserin-treated compared to placebo-treated patients reported meaningful improvements in satisfying sexual events, sexual desire, or distress. The most common adverse effects were dizziness, somnolence, nausea, and fatigue [13–15]. Several weeks may be required to see clinical benefit, and clinicians should discontinue treatment after 8 weeks if there is no response. While some studies showed positive benefits in postmenopausal women, researchers have not evaluated flibanserin use in women with DM. Therefore, clinicians should weigh the modest benefits against the side effects and cost of the medication in women with DM.

Clinicians have tried oral, injectable, and transdermal testosterone in women with HSDD [16], but these remain off-label. See Table 3. Testosterone increases sexual desire and

satisfaction in women who are naturally postmenopausal, surgically postmenopausal, and premenopausal with HSDD. Hirsutism and acne are common adverse effects in women, but the transdermal formulation is associated with lower rates or no difference when compared to placebo [16]. The Endocrine Society recommends a 3- to 6-month trial of testosterone in postmenopausal HSDD women with no contraindications [17]. Clinicians should monitor testosterone levels at baseline, after 3–6 weeks of therapy, and monitor for signs of androgen excess [17]. Long-term studies are still needed to assess the risk of breast cancer, changes in lipid levels, and the development of cardiovascular disease.

Bupropion has been used off-label for HSDD. Two clinical trials showed improvement in sexual function with bupropion sustained release 150 and 300 mg once daily [18]. The most commonly reported adverse effects include headache, insomnia, dry mouth, and nausea [18, 19]. Sildenafil has shown improvements in FAD, but not HSDD [18]. Buspirone showed an improvement in sexual function in patients taking an SSRI for depression, who were

Table 3 Treatment options for HSDD (including off-label medications) [12–19]

Treatment	Indications
Flibanserin (Addyi [®])	FDA-approved for generalized acquired HSDD in premenopausal women
Testosterone (oral, injectable, and transdermal)	Off-label, but increases sexual desire and satisfaction in pre- and postmenopausal women with HSDD
Bupropion (Buspar [®])	Off-label, but can improve sexual function
Sildenafil (Viagra [®])	Not effective for HSDD. Some improvement in FAD
Alternative therapies: DHEA, ginkgo biloba, L-arginine	Limited data regarding effectiveness

FAD female arousal disorder, *HSDD* hypoactive sexual desire disorder

also experiencing sexual dysfunction [6]. There is currently no evidence to support the use of buspirone for HSDD.

Alternative therapies such as DHEA, ginkgo biloba, ginseng, and L-arginine have limited data regarding their effectiveness [18]. As a result of their lack of evidence, improving glycemic control needs to be the initial goal to increase sexual desire.

CONCLUSIONS

HSDD is a multicausal, multidimensional problem combining biological, psychological, and interpersonal elements. Clinicians should proactively evaluate women with DM early for risk factors as part of their clinical evaluation. Clinicians should offer women with HSDD a multidisciplinary approach with a combination of vaginal lubricants, flibanserin, hormonal therapy, and/or psychological counseling for management. Clinicians need more studies in women with DM and HSDD to guide them in optimal therapy.

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Data Availability. Data sharing is not applicable to this article as no datasets were generated or analyzed during the current study.

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