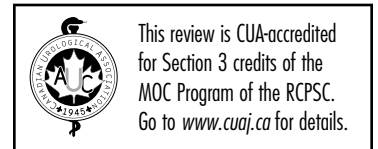


A practical guide to female sexual dysfunction: An evidence-based review for physicians in Canada



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Cite as: *Can Urol Assoc J* 2018;12(6):211-6. <http://dx.doi.org/10.5489/cuaj.4907>

Published online February 23, 2018

Introduction

The evaluation and treatment of male sexual dysfunction has developed considerably since the release of sildenafil (Viagra®) as a treatment for erectile dysfunction in 1998.¹ There is a societal perception that it is important for men to preserve their sexual function and optimize their sexual performance. This perception, coupled with perpetual innovation in male sexual medicine, has led to many treatment options for male sexual dysfunction, including oral therapies for erectile dysfunction, multiple vehicles for hormonal replacement, shockwave therapy, and penile implants for refractory erectile dysfunction. There are fellowships throughout Canada dedicated to the medical and surgical management of male sexual dysfunction. Medical students and residents across many disciplines are routinely exposed to the evaluation and treatment of men with sexual dysfunction. Unfortunately, despite robust clinical and academic interest in male sexual dysfunction, women with sexual complaints have been largely overlooked.² There have been limited treatment options, few Canadian role models who specialize in female sexual medicine, and little academic activity in the area of female sexual function.

Fortunately, over the past decade there has been an increase in the clinical and academic interest in female sexual function. The times appear to be changing. The International Society for the Study of Women's Sexual Health (ISSWSH) was established in 2001 to serve as a multidisciplinary international community dedicated to advancing the study of female sexuality. There are published guidelines and position papers that reinforce the practical aspects of female sexual dysfunction (FSD) evaluation and management.³ There has been an important increase in research regarding the impact of cancer and its treatment on female sexual function.⁴ And

finally, there are now U.S. FDA-approved therapies for both low desire and sexual pain that will possibly be available in Canada in the future.⁵⁻⁷ The increase in attention to female sexual function over the past decade can be attributed to a number of factors, including the establishment of ISSWSH, new treatments offering hope, an increase in female sexuality research, and broader societal forces promoting equity in medical practice and research.

This review provides a practical, evidence-based guide to the evaluation and management of FSD that is adaptable for clinical practice in Canada.

For the purpose of this review, the classification of FSD have been divided into four broad categories: sexual pain, low desire, low arousal, and orgasmic dysfunction. These closely mirror the DSM V classifications of FSD, comprised of: genito-pelvic pain/penetration disorder (sexual pain), female sexual interest/arousal disorder (low desire and low arousal), and female orgasmic disorder (orgasmic dysfunction).⁸ These classifications have been chosen instead of the DSM classifications, as many patients will not meet strict criteria but will still benefit from evaluation and management. A symptom-based approach is the most effective means to organize the initial medical evaluation and treatment of women with sexual complaints to encourage collaboration and communication between healthcare providers.

Evaluation and treatment of female sexual dysfunction

1. Sexual pain

Evaluation

Sexual pain is a common complaint in women of all ages and may include pain at the vulva, deep pain with penetration, or tightening of the pelvic musculature. A complete medical history should include a gynecological history, medication review, history of birth control or hormonal therapy use, and a psychosocial history, including a screen for mood disorders and abuse (Table 1). Standardized sexual function surveys, such as the Female Sexual Function

Inventory (FSFI), are an efficient way to assess patients at baseline and followup.⁹ Physical exam should include vulvoscopy, if possible, to document skin changes, specific points of sensitivity, labial measurements, assessment of the clitoris and clitoral hood, and a thorough assessment of the pelvic muscles with an internal exam. Vulvoscopy with high-definition projected images allows patients to appreciate the anatomical changes that may be contributing to their symptoms. Q-tip testing at the vulva and vestibule may identify specific areas of tenderness that can be documented and reassessed at followup. Documenting baseline vaginal pH and followup values can determine if treatment has been effective, as patients with atrophic vaginitis will often demonstrate elevated vaginal pH that will normalize with local hormonal therapy. Vulvar biopsy may be necessary to definitively diagnosis dermatological abnormalities (such as lichen sclerosis and lichen planus) as a cause of vulvar pain.

Patients who experience vulvar pain without an obviously identifiable cause (referred to as vulvodynia) can be further classified based on history and physical exam. Some patients may exhibit reproducible provoked pain (provoked vulvodynia) while others may have generalized vulvar pain (generalized vulvodynia). Patients may describe a history of deeper pelvic pain and demonstrate pelvic floor muscle abnormalities on internal exam. It is important to systematically document the findings on physical exam to establish a diagnosis and follow progress once treatment is initiated.

Laboratory investigations can help identify patients with endocrine abnormalities (thyroid-stimulating hormone, prolactin) and those with hormonal deficiencies (estradiol [E2], total testosterone [TT], sex hormone-binding globulin [SHBG], and calculated free testosterone [cFT]). It is recom-

mended to measure the patient's TT and to use a standardized calculation to calculate the patient's cFT — the amount of testosterone that is actually free to exert physiological effects.¹⁰ Some women may demonstrate a low cFT that can contribute to sexual pain, low libido, low arousal, and orgasmic dysfunction.¹¹ In women on hormonal contraception, elevations of SHBG (that tightly bind to testosterone and render it biologically inactive) and decreased ovarian production of testosterone can lead to significantly deficient levels of cFT despite normal TT values. The vulvar vestibule is rich in androgen receptors and some patients may be at a higher genetic risk from experiencing pain related to low levels of testosterone.¹² Symptoms of vulvovaginal irritation in the context of low hormones states are commonly referred to as hormonally mediated vulvodynia. Menopausal women may experience similar symptoms from atrophic vulvovaginitis secondary to a low estrogen state.¹³

Treatment

Treatment is patient-specific and requires a multidisciplinary team. Pelvic physiotherapy is often needed to improve pelvic floor muscle dysfunction that may present a primary condition or be secondary to prolonged vulvar pain. A 2017 systematic review of 43 studies, including seven randomized control trials, demonstrated significant reduction in pain and improvement in sexual function with pelvic physiotherapy.¹⁴

A retrospective review from 2010 demonstrated that 25 of 26 patients experienced statistically significant improvement when physiotherapy was combined with vaginal and/or rectal suppositories.¹⁵ Studies are now reporting on improvements from pelvic floor onabotulinumtoxin A therapy.¹⁶ Most high-volume centres collaborate closely with pelvic physiotherapists.

Many clinicians address vulvar pain prior to treating pelvic muscle floor dysfunction as superficial vulvar pain, which may make pelvic physiotherapy exceedingly difficult. Pain at the vulva may be related to low hormone states, which are commonly associated with oral contraception use or menopause. This can be treated by switching to another form of contraception and the use of vestibular and vaginal hormonal therapy in the form of estrogen or a mixture of estrogen and testosterone. Studies have demonstrated improvements with combination estrogen/testosterone topical therapy.¹⁷ The recently released North American Menopause Society (NAMS) guideline is a helpful resource for managing patients with genitourinary syndrome of menopause related to low estrogen.¹³ It is important to note that patients with hormone-sensitive breast cancer (especially those on hormonal-suppressing therapies) are a unique cohort that require collaboration between the patient, sexual health provider, and oncologist.¹⁸ Treatment of vulvar pain in hormone-sensitive breast cancer patients should begin with non-hormonal therapies.¹³ A recent study reported that intravaginal testosterone and estradiol-releasing vaginal rings

Table 1. Initial approach to patients with female sexual dysfunction	
History	History of presenting illness Sexual history Complete gynecological history Birth control and hormone therapy history Medications Psych history Standardized Screener (e.g., FSFI)
Physical exam	General appearance Abdominal exam Vulvoscopy Presence of dermatological lesions (± biopsy) Cue tip testing for vulvodynia Vaginal pH for atrophic vaginitis Microscopy/KOH testing for clue cells, parabasal cells
Investigations	TSH, prolactin Sex hormone-binding globulin Estradiol Total testosterone Calculated free testosterone

FSFI: Female Sexual Function Inventory; TSH: thyroid-stimulating hormone.

demonstrated a favourable safety profile in the short-term in women on aromatase inhibitors.¹⁹ However, there is no robust data to suggest safety of local hormonal therapy in this cohort of patients, and both providers and patients need to be aware of the uncertainty and potential risk.

Skin lesions suspicious for cancer or autoimmune diseases should be biopsied for definitive diagnosis. Lichen sclerosis and lichen planus are common vulvar conditions that are amenable to topical therapy.²⁰

There are a number of non-hormonal treatments that have demonstrated success in the treatment of vulvodynia. A 2004 case series demonstrated significant benefit in 19 of 32 patients treated with topical lidocaine followed by 0.05% topical capsaicin.²¹ A 2003 case series of premenopausal women with provoked vulvodynia showed a greater than 50% decrease in sexual pain in over half of patients treated with 5% topical lidocaine ointment for 6–8 weeks.²² A randomized control trial of 46 patients with a history of breast cancer and low estrogen demonstrated improved pain scores and a resumption of sexual activity in 85% of patients that applied liquid lidocaine prior to penetration.²³

Refractory and severe cases of vulvodynia can ultimately be managed surgically with the resection of vestibular tissues with posterior vaginal advancement flap (vestibulectomy). A cohort of 31 patients recently demonstrated a 60–70% reduction in pain scores following vestibulectomy.²⁴ In a larger cohort of 134 patients treated with vestibulectomy, 93% reported being satisfied or very satisfied with the outcome.²⁵

There has been a recent increase in the marketing of minimally invasive technology aimed at improving vulvovaginal atrophy and associated sexual pain. The cost of these treatments is not currently covered by provincial health plans. A randomized, double-blinded, placebo-controlled trial of fractionated CO₂ demonstrated benefits to pain scores, vaginal burning, and vaginal dryness.²⁶ Satisfaction rates were demonstrated to be above 90% in a cohort study of patients with vulvovaginal atrophy treated with fractionated CO₂.²⁷ A recent review demonstrated significant improvements in pain scores and sexual function across six studies with a total of 273 women.²⁸ Evidence for vaginal laser treatment is new and its role in patient management is currently unclear. Some advocate for this new technology for women who wish to avoid hormonal therapies.²⁹ As studies continue to report outcomes and adverse events associated with treatment, patients will be able to weigh the risks and benefits of these new treatments in the management of sexual pain and vulvovaginal atrophy.

2. Low desire

Evaluation

Women with low desire will experience an absence or reduction in sexual fantasies and desire for sexual activ-

ity that causes distress. Sexual desire is fluid throughout a lifetime, however, at various points in one's life, low sexual desire may cause significant distress. Like painful sex, evaluating and treating women with low desire requires a multidisciplinary approach that includes medical and psychosocial assessments.

A thorough medical history that focuses on the psychosocial factors that may impact one's sexual desire is critical. A review of relevant medications is important, as certain therapies may cause decreased sexual desire (Table 2). Hormonal contraception has been linked to low desire.³⁰ Hormonal assessment should include an E2 level, SHBG, TT, cFT, prolactin, and thyroid-stimulating hormone (TSH). It is important to try to ascertain if the low desire is acquired or lifelong, and whether it is situational or generalizable (Table 3), as some treatment options will depend on this distinction.

Treatment

A multidisciplinary approach to low desire is important. There are a number of medical treatments with evidence to support their use in patients with low desire. In the U.S., flibanserin (Addyi®) has been approved for the treatment of low desire in premenopausal women with acquired, generalized low desire.³¹ Studies have also demonstrated efficacy and safety in post-menopausal women as well, although this still constitutes off-label usage.³² There is also evidence for the use of central nervous system medications for their pro-dopamine effects as a treatment for patients with sexual side effects from selective serotonin reuptake inhibitors (SSRIs).³³ High-dose bupropion (150 mg twice daily) has been shown to be an effective treatment for SSRI-related sexual dysfunction.³⁴

The Endocrine Society recommends a trial of testosterone therapy for 3–6 months in postmenopausal women with low androgen levels that are comfortable with off-label use and close monitoring.³⁵ A 2008 double-blinded, randomized, controlled trial of 814 women demonstrated that systemic testosterone therapy improved desire and reduced distress in women with low desire.³⁶ A 2017 meta-analysis of postmenopausal women with low desire treated with systemic testosterone (n=3035) demonstrated statistically significant improvements in sexual desire, orgasm, and sexually satisfying events.³⁷ The most recent ISSWSH consensus panel suggests that post-menopausal women with low desire may benefit from a trial of systemic testosterone.³⁸ Despite the evidence of testosterone therapy's efficacy and short-term safety, it is important to note that testosterone treatment is off-label and that there are currently no pharmaceutical formulations made for female doses or application.

Table 2. Medications impacting female sexual function

Class	Examples
Psych/neuro	Selective serotonin reuptake inhibitors Benzodiazepines Lithium Antipsychotics Phenytoin
Hormonal	Contraception Anti-androgens Tamoxifen Aromatase inhibitors Ketoconazole
Pain	Opioids Tricyclic antidepressants Indomethacin
Cardiovascular	Spironolactone Digoxin Methyldopa Beta blockers Clonidine

3. Low arousal

Evaluation

A number of women will present to their healthcare providers with symptoms related to low arousal that may manifest as a decrease in vaginal lubrication and a decrease in genital warmth related to blood flow. As above, a full medical and sexual history and physical examination are critical. Comorbid conditions that may impact arousal should be documented, as should a complete list of medications. Hypertension, hyperlipidemia, and diabetes have all been linked to FSD and low arousal states.^{39,40} A multidisciplinary team consisting of a medical provider, psychosocial support, and pelvic physiotherapist can all contribute to the evaluation of a patient with low arousal.

Treatment

The management of comorbid conditions, such as diabetes and hypertension, should be optimized.⁴¹ Offending medications may be dose reduced and/or replaced with less sexually inhibiting alternatives if possible. There has been mixed evidence that phosphodiesterase inhibitors may benefit women with poor arousal (by improving pelvic blood flow) and a trial of on-demand phosphodiesterase type 5 inhibitor may be of benefit for some women.⁴² A 2016 randomized controlled trial of 86 women favoured cognitive behavioural therapy over phosphodiesterase inhibitor usage for the treatment of low arousal.⁴³ A 2003 randomized, double-blind study of 34 patients failed to show any significant benefits from oral sildenafil in women with low arousal.⁴⁴ The conflicting evidence on the role of phosphodiesterase inhibitors in women with low arousal appears to suggest that patients with arousal disorder are a heterogeneous group of patients and only some may benefit from its use.

Table 3. Classification of low sexual desire

Menopausal status	Premenopausal vs. postmenopausal
Onset	Lifelong vs. acquired
Situation	Situational vs. generalized

4. Orgasmic dysfunction

Evaluation

For women complaining of distress related to delayed or absent orgasms, it is necessary to take a detailed medical and psychosocial history, and to identify possible offending medications. Understanding if the problem is lifelong or acquired and distinguishing between completely absent orgasms and delayed or less intense orgasms are important points in the sexual history that will guide medical and psychosocial treatment. Similar to the approach for low libido, clinicians must also identify if the problem is situational or acquired. All of these distinctions, elucidated on a thorough sexual history, aid both the psychosocial and medical treatment of orgasmic dysfunction. Orgasmic dysfunction is often associated with other forms of sexual dysfunction; for example, patients with sexual pain and poor arousal will often find it difficult to reach orgasm. The evaluation should, therefore, put the orgasmic dysfunction in context of an individual's broader sexual function. Physical exam, including vulvoscopy, should include an assessment of the clitoris. Some women may exhibit phimosis (covering) of the clitoris with or without an underlying etiology (such as lichen sclerosis). Patients should also be screened and examined for female genital mutilation, which often involves damaging the external portion of the clitoris.

Treatment

The medical treatment of orgasmic problems is challenging, although there have been reports of success with mindfulness, yoga, the use of sex toys, and sex therapy.⁴⁵ Directed masturbation has demonstrated efficacy for women with lifelong anorgasmia.⁴⁶ As previously noted, SSRIs have been linked to delayed or absent orgasms and can be dose reduced, replaced with other psychiatric medications, or combined with bupropion. Some clinicians have experimented with the off-label use of testosterone, dopamine agonists, and yohimbine hydrochloride with encouraging results, although there are no clinical trials to currently support their usage. A randomized controlled trial published in the *Journal of the American Medical Association* demonstrated that sildenafil improved orgasm in women on SSRIs better than placebo.⁴⁷ Small cohort studies have shown high patient satisfaction rates with surgery or CO₂ laser treatment in patients with clitoral phimosis.^{48,49}

Table 4. Summary of diagnosis and treatment of female sexual dysfunction

Diagnosis	Treatment
Sexual pain	Local hormone therapy Counselling Pelvic physiotherapy Vaginal/rectal suppositories Topical lidocaine Capsaicin Vestibulectomy
Low desire	Hormonal therapy Counselling Bupropion Flibanserin (not available in Canada)
Low arousal	Hormonal therapy Counselling PDE5 inhibitors (e.g., sildenafil)
Orgasmic dysfunction	Mindfulness, sex therapy Hormonal therapy Bupropion PDE inhibitors (e.g., sildenafil) Yohimbine hydrochloride

PDE: phosphodiesterase.

Conclusion

There is a strong basis for the evidenced-based evaluation and management of FSD. A basic understanding of the common presentations, evaluation, and medical management of FSD can empower primary care providers to inquire about sexual symptoms and offer an appropriate workup and initial treatment (Table 4). A common and multidisciplinary approach to FSD promotes better communication and outcome.

Competing interests: Dr. Krakowsky has attended advisory boards for Acerus, AMS/Boston Scientific, and Paladin. Dr. Grober has attended advisory boards for Acerus, Apotex, Mylan, and Paladin.

This paper has been peer-reviewed.

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