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

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Abstract

Introduction: Female sexual dysfunction (FSD) is characterized as distress related to sexual pain, sexual arousal, sexual desire, and/or orgasmic dysfunction. Despite prevalence rates similar to male sexual dysfunction, women with sexual complaints have been long under-evaluated, treated, and studied. Over the last decade there have been advances in the medical evaluation and management of FSD, however, there remains a paucity of clinical resources available for women in Canada with sexual dysfunction.
Methods: The state of knowledge in the evaluation and treatment of FSD was reviewed. Recommendations are given for the practical evaluation and treatment of women with sexual symptoms that can be applied widely in Canada.
Results: Approaches to the management and treatment of FSD are discussed with a focus on the practical application of diagnostic and therapeutic tools in the management of sexual pain, low desire, low arousal, and orgasmic dysfunction.
Conclusions: There are evidence-based diagnostic and therapeutic approaches to FSD that can be broadly applied by Canadian physicians to improve access to female sexual medicine in Canada.

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 has 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 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 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 which closely mirrors the DSM V classifications of FSD, compromised 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 survey such as the Female Sexual Function Inventory (FSFI) are an efficient way to assess patients at baseline and follow-up.[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 allow patients to appreciate the anatomic changes that may be contributing to their symptoms. Cue tip testing at the vulva and vestibule may identify specific areas of tenderness that can be documented and reassessed at follow-up. 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 systemically 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 recommended 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 physiologic 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 biological 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 PT is often needed to improve pelvic floor muscle dysfunction that may present a primary condition or secondary to prolonged vulvar pain. A 2017 systematic review of 43 studies, including 7 randomized control trials, demonstrated significant reduction in pain and improvement in sexual function with pelvic physiotherapy.[14]

A retrospective review from 2010 demonstrated that 25/26 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 PT.

Many clinicians address vulvar pain prior to treating pelvic muscle floor dysfunction as superficial vulvar pain may make pelvic PT 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 with 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 supressing 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 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 on 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 vestublectomy, 93% reported being satisfied or very satisfied. [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 are 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 weight 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 activity 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 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, mentioned below, 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 United States, 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 SSRI.[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 T therapy for three to six months in postmenopausal women with low androgen levels that are comfortable with off-label use and close monitoring.[35] A 2008 double blinded randomized control trial in 814 women demonstrated that systemic testosterone therapy improved desire and reduced distress in women with low desire.[36] A 2017 meta-analysis of post-menopausal 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.

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 is critical. Comorbid conditions that may impact arousal and should be documented as well as a complete list of medications. Hypertension, hyperlipidemia and diabetes have all been linked to FSD and low arousal states. [39,40] A multidisplinary team consisting of a medical provider, psychosocial support and pelvic PT 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 have been mixed evidence that phosphodiesterase inhibitors may benefit women with poor arousal (by improving pelvic blood flow) and a trial of on-demand PDE5 may be of benefit for some women.[42] A 2016 randomized control trial of 86 women favoured cognitive behavioral therapy over PDEI usage for the treatment of low arousal. [43] A randomized double blind study of 34 patients from 2003 failed to show any significant benefits from oral sildenafil in women with low arousal [44] . The conflicting evidence on the role of PDEI in women with low arousal appears to suggest that the patients with arousal disorder are a heterogenous group of patients and some may benefit from PDEI.

4. Orgasmic dysfunction

Evaluation

For women complaining of distress related to delayed or absent orgasms it is necessarily to take a detailed medical history, psychosocial history and 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 the medical and psychosocial treatment. Similar to the approach to low libido clinicians must also identify if the problem is situational or acquired. All of these distinctions that are 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 has 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 SSRI have been linked to delayed or absent orgasms and can be dose reduced, replaced with other psychiatric medications or combined with buproprion. 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 control trial published in the Journal of the American Medical Association demonstrated that sildenafil improved orgasm is women on SSRIs better than placebo.[47] Small cohort studies have shown high patient satisfaction rates in patients with clitoral phimosis underoing surgery or CO2 laser treatment[48,49].

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 (see table 4). Sharing a common approach to FSD allows easier communication among patients and between healthcare providers.

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Figures and Tables

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.

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

Table 3. Classification of low sexual desire	
Menopausal status	Premenopausal vs. postmenopausal
Onset	Lifelong vs. acquired
Situation	Situational vs. generalized

Table 4. Summary of diagnosis and treatment of female sexual dysfunction	
Diagnosis	**Treatment**
Sexual pain	Local hormone therapy Counselling Pelvic PT Vaginal/rectal suppositories Topical lidocaine Capsaicin Vestibulectomy
Low desire	Hormonal therapy Counselling Buproprion Flibanserin (not available in Canada)
Low arousal	Hormonal therapy Counselling PDE5 inhibitors (e.g., sildenafil)
Orgasmic dysfunction	Mindfulness, sex therapy Hormonal therapy Buprioprion PDE inhibitors (e.g., sildenafil) Yohimbine hydrocholoride

PDE: phosphodiesterase; PT: physical therapy.