Screening and Management of Female Sexual Dysfunction During the Second Half of Life

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10.1 Introduction

Female sexual dysfunctions (FSDs) are common, affecting 25–43% of women, with lack of desire being the most prevalent. Perimenopausal women report lubrication problems, less sexual participation, orgasm problems, absence of sexual fantasies, less sexual gratification, and decreased sexual interest and activity [1]. FSD increases threefold during climacteric years and is more evident after age 60. Female sexuality is a complex process influenced by many personal and partner factors that may negatively affect quality of life. Although one third to one half of mid-aged women display some degree of sexual problems related to aging and hormonal status, determinant factors may vary according to the studied population, study design, and the used approach [2]. Consequently, clinicians who take care of women should evaluate promptly when they may be vulnerable to sexual dysfunction.

FSD has been linked to the following risk factors: poor physical and mental health, postmenopausal status, stress, genitourinary complaints, sexual abuse, bad relationships, religious beliefs, bad economic conditions, intimate partner violence,

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partner's age, and male sexual dysfunctions (premature ejaculation and/or erectile dysfunction) [3, 4]. Contrarily, protective factors include older age at marriage, partner faithfulness, menopausal hormone therapy, exercise, daily affection, intimate communication, having a positive body image or self-esteem, and the use of hormonal contraception [2, 4–6].

The Fourth International Consultation on Sexual Medicine (ICSM) defined female and male sexual dysfunctions, prevalence, and the risk factors according to the opinion of experts and to current and strong supporting literature [7]. Section 17 of the *International Classification of Diseases (ICD) 11 for Mortality and Morbidity Statistics* defines sexual dysfunctions as syndromes in which adults may have difficulty having satisfying, noncoercive sexual activities [8]. Both organizations used the term FSD.

The fifth edition of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-5) classifies female sexual disorders as orgasmic disorder, sexual interest/arousal disorder, and genito-pelvic pain/penetration disorder. The DSM-5 further includes four specific subtypes to categorize the onset of dysfunction: (1) lifelong dysfunction indicating a sexual problem present from the first sexual experience, (2) acquired dysfunction identifying sexual health issues that arise after a time of normal sexual activity, (3) generalized dysfunction referring to sexual issues not limited to a specific situation or partner, and (4) situational dysfunction which occurs with specific partners or situations [9]. Despite this, diagnostic criteria require more precision than before; thus, diagnosis of sexual dysfunction requires the duration of at least 6 months and a frequency of 75–100%. Thus, disorders must cause significant distress, and the "interpersonal difficulty" from the DSM-4 definition has been deleted (American Psychiatric Association, DSM 2013 [9]). The present review will use the old and new nomenclature in order to respect the original articles.

10.2 Screening of Female Sexual Dysfunction

During sexual assessment, questions have to be specific, no assumptions have to be made, and a semi-structured interview is recommended [10]. Common questions that may be included are detailed in Table 10.1. The objectives of the sexual history are identifying the predisposing, precipitating, and maintaining factors of sexual symptoms. Menopausal women have the same sexual concerns as young people,

Table 10.1 Common questions in a semi-structured interview (sexual history)

How often do you feel like having a sexual experience?
Are there any situations that help you feel excited?
Do you remember having any sexual fantasy?
Do you ever have erotic dreams?
Do you feel pleasure with sexual activities? Can you explain what you feel?
What do you think has had an influence in the changes you are experiencing in your sexual function?
How long has it been a problem for you?

and no aspects of sexuality should be avoided [11]. It is recommended to ask about women's current relationship and about partner's possible sexual problems.

Regarding postmenopausal women, Cuerva et al. [12] have suggested to initially omit issues relating to sexuality, unless these are raised by the patient. Then, after 5 min, the gynecologist may offer the possibility of talking about sexuality and ask about possible sexual problems. Using this approach in Spanish women, it was found that 12.1% reported sexual problems during the first 5 min of the interview. However, patients with sexual issues increased to 48.0% when they were asked about sexuality after 5 min. The main factors associated with having a sexual problem were the genitourinary syndrome of menopause (GUSM) and having a stable sexual partner. Therefore, openly asking postmenopausal women about sexuality in gynecological consultations increases the number of diagnoses of sexual problems [12].

Clinicians can also screen women, regardless of age, with the help of a validated sex questionnaire or during a routine review of systems. There are many validated screening tools available. We will briefly mention those which provide a comprehensive assessment of female sexuality and those used to search specific sexual disorders. A high prevalence of different sexual dysfunctions has been reported by using these questionnaires as well as correlations with female sociodemographic and health factors and partner health status and behavior.

10.2.1 Changes in Sexual Functioning Questionnaire

The original Changes in Sexual Functioning Questionnaire (CSFQ) is a test that includes 36 items identifying 5 scales of sexual function [13]. The abridged CSFQ of 14 items (CSFQ-14) provides information about sexual desire, arousal, and orgasm. The tool shows construct validity as a global measure of sexual dysfunction, and the individual scales have internal reliability [14].

In Spanish women aged 40–59 years, higher total CSFQ-14 scores (better sexual function) were correlated with better satisfaction with life and inversely correlated to female age and worse menopausal symptoms. The satisfaction with life score correlated with the total CSFQ-14 score and body mass index (BMI) and inversely correlated with economic problems, female tobacco use, lack of healthiness, menopausal symptoms, not having a partner, and partner's lack of healthiness [15].The prevalence of sexual dysfunction (CSFQ-14 score ≤41) was 46% (premenopausal and postmenopausal). Worse sexual function was associated with severe menopause symptoms, low satisfaction with life, and economic problems [15].

About 64.1% of Spanish postmenopausal women (median age 57 years, 17.1% with hypertension, 66.7% with increased BMI, and 48.7% with depressive mood) displayed CSFQ-14 total scores ≤41, suggesting sexual dysfunction. In addition, CSFQ-14 total scores inversely correlated with quality of life (total, psychological, and urogenital), and arousal sub-scale scored inversely with global quality of life and urogenital symptoms and orgasm with the global quality of life. In this postmenopausal sample, sexual function correlated with female educational level and

partner education and regular exercising. There is also an inverse correlation between CSFQ-14 score and depressed mood [16].

10.2.2 Female Sexual Function Index

The Female Sexual Function Index (FSFI) assesses sexual function of the past 4 weeks. It is composed of 19 questions (FSFI-19) grouped in 6 domains or dimensions: desire (items 1 and 2), arousal (items 3–6), lubrication (items 7–10), orgasm (items 11–13), satisfaction (items 14–16), and pain (items 17–19). Each question can be scored in a Likert fashion from 0 to 5. Higher scores indicate better sexual function [17]. Subsequently, Wiegel et al. [18] determined a cutoff value for the FSFI-19 for the definition of FSD (total FSFI-19 scores of 26.55 or less). Indeed, using this cutoff value, it was found that 70.7% of women with sexual dysfunction and 88.1% of the sexually functional ones were correctly classified. The original FSFI-19 has been validated in several languages. It has been used to assess sexuality of pre- and postmenopausal women and among different ethnical populations and different medical conditions, all displaying good reliability values. Its utility has also been proven in a longitudinal cohort of pre-/postmenopausal British women in whom the main predictors of changes in sexual functioning and satisfaction were desire and arousal [19].

A six-item abridged version (FSFI-6) was developed by Isidori et al. [20] covering desire (original item #2), arousal (original item #4), lubrication (original item #7), orgasm (original item #11), satisfaction (original item #16), and pain (original item #17). Each item is scored as the original FSFI-19. The sensitivity and specificity were 0.93 and 0.94, respectively, at the cutoff of 19 or less. The Spanish language version of the FSFI-6 has been used to study mid-aged Spanish women [1, 2]. Upon multivariate analysis, total FSFI-6 scores positively correlated with both female and partner education and inversely (worse sexual function) with female age, partner alcohol consumption and erectile dysfunction, and total Hospital Anxiety and Depression Scale (HADS) scores and urogenital and somatic symptoms [2].

10.2.3 Decreased Sexual Desire Screener

The Decreased Sexual Desire Screener (DSDS) was specifically developed for use by clinicians not experienced in sexual medicine [21]. It is a five-question self-administered survey that helps identify in a time-efficient manner women with generalized acquired hypoactive sexual desire disorder (HSDD). The DSDS is brief, effective, and self-completed and requires no special training for its application and/or interpretation. The screener includes five simple "yes/no" questions. The first four incorporate the prerequisites for a diagnosis of generalized acquired HSDD: (1) previous satisfaction with her desire/interest in sex; (2) a decrease from prior satisfaction; (3) bothered by the decline in sexual desire; and (4) wish for the improvement of her sexual desire [22]. Responses of no previous satisfaction with

her desire or interest in sex and therefore no decrease from prior satisfaction would be consistent with lifelong low sexual desire or interest. In the fifth item, the patient is asked to identify with "yes or no" responses which, if any, of the seven listed group of factors might apply to her situation, potentially having an adverse effect on her sexual desire/interest [21].

Low sexual desire and the associated distress and behavioral adaptations may impact the partner relationship, or problems in the partner relationship may contribute to low desire. If a woman responds "no" to at least one of the first four questions, then she does not meet the criteria for generalized acquired HSDD but could meet the criteria for either situational or lifelong low sexual desire/interest. If the patient answers "yes" to questions 1 through 4 and "no" to all the factors in question 5, she has generalized acquired HSDD. If any of the factors in question 5 are present, the healthcare provider must evaluate and consider differential diagnoses including biological etiologies of low desire as well as decide whether the responses to question 5 indicate generalized acquired HSDD or situational low sexual desire/interest.

If the DSDS suggests the diagnosis of low sexual interest without distress, distressing lifelong sexual desire, or situational low sexual desire, the healthcare provider should consider strategies that engage education and/or counseling or referral to a specialist. In those with generalized acquired HSDD, the healthcare provider may elicit a sexual history or proceed with the process of care [23].

10.2.4 Screening Tests for Women Who Have Sex with Women

Women who have sex with women may also have sexual dysfunction. Shindel et al. [24] used a modified version of the FSFI-19 to evaluate sexual function in women who have sex with women. This was an Internet-based survey that showed that 24.8% of participants presented FSD, which upon multivariable analysis was independently associated with subjective bothered sexual function, overactive bladder, and having a non-female partner or no partner. In addition, FSFI scores, for all domains (but not desire), were negatively affected by the partner factors and overactive bladder.

10.3 Clinical Assessment of Female Sexual Dysfunction

The clinical assessment of FSD starts by a general approach to women's intimacy-related issues and sexual concerns. When working with special patients like menopausal women, it is convenient also asking about how their specific conditions may affect their sexuality. Specific conditions that may be present in relation to the menopause and can affect sexuality are vasomotor symptoms and the GUSM, pelvic floor disorders, metabolic disorders (overweight or diabetes), adverse mood (depression, anxiety, and perceived stress), or sleep disorders.

The diagnosis of FSD is based on medical and sexual history and self-reports (through questionnaires or diaries) [10]. It should include a comprehensive clinical

interview. The medical history is orientated to identify organic, psychological, and medication issues affecting sexuality. Physical examination is only mandatorily required for sexual pain disorders; however, it may help in every sexual dysfunction at least to confirm normal anatomy and the absence of concurrent gynecological diseases like GUSM or pelvic floor disorders. Laboratory tests are not routinely recommended for the evaluation of FSD. Circulating hormone levels poorly correlate with the assessed sexual function. Androgens, estrogens, and prolactin, among other hormones, are known to be involved in sexuality, but their levels are not independent predictors of women's sexual function. The increase in the prevalence of FSD in the context of menopause shows the important correlation between hormonal status and sexual function, but treatment based only on hormonal therapy does not revert the rise in FSD prevalence. Furthermore, partners of mid-aged women may also have sexual dysfunction and/or work or social issues that may in fact be more negative than hormonal changes as a cause of FSD.

10.4 Female Sexual Function and Comorbidity During the Second Half of Life

Both peri- and postmenopausal women need a detailed gynecologic examination that includes the assessment of (1) pelvic floor disorders such as urinary incontinence, fecal incontinence, prolapse, and high-tone pelvic floor dysfunction and (2) menopausal vasomotor symptoms and emotional changes (depressive symptoms, anxiety, perceived stress, fatigue) because each has been associated with decreased sexual desire [25].

10.4.1 Menopause and Sexuality

Postmenopausal estrogen loss typically leads to vulvovaginal atrophy and dryness, as well as changes in genital function via reduced clitoral blood flow and decreased sensory perception. Genital estrogen application may reduce the negative effect of menopause, if initiated in the early postmenopausal years/time [26, 27]. In the Real Women's Views on Treatment Options for Menopausal Vaginal Changes study, 63% of women with symptomatic vulvovaginal atrophy reported that their symptoms interfered with enjoyment of sexual intercourse, and 47% of partnered women indicated it interfered with their relationship [28]. Twelve percent of women without a partner reported that they were not seeking a sexual partner because of symptoms related to vulvovaginal atrophy [29]. More intense vulvovaginal symptoms were positively related with biological conditions such as surgical menopause, sexual inactivity, economic problems, urinary incontinence, and the use of phytoestrogens [30].

Menopause has long been assumed to result in decreased desire due to the decline in ovarian testosterone production and estrogen loss. It has also been theorized that

fluctuations in testosterone levels lead to decreased libido [31]. Circulating estrone sulfate (E1S) and androsterone glucuronide (ADT-G) are the main metabolites of estrogens and androgens in postmenopausal women. In postmenopausal women, estrogens and androgens are synthesized from circulating dehydroepiandrosterone sulfate (DHEA) and the vagina layers and nerve density [32]. Postmenopausal women who do not have vulvovaginal symptoms in fact have 16% higher levels of the mentioned metabolites as compared to those reporting moderate to severe symptoms. In addition, estrone serum levels are 14.5% higher in asymptomatic women as compared to those without vulvovaginal atrophy [33]. These endocrine aspects are pivotal for low genital tract health and postmenopausal vulvovaginal atrophy; its correction may improve sexuality.

Bilateral salpingo-oophorectomy at any age is associated with lower total and free testosterone levels. Women should be asked about other pelvic operations, trauma, or radiotherapy because these may be associated with pelvic pain and altered ovarian function. Other conditions associated with lower androgen levels are less frequent than oophorectomy, and potentially diminished desires include hyperprolactinemia and hypopituitarism, adrenal insufficiency, primary ovarian insufficiency, and chemical ovarian suppression. Conditions that may increase sex hormone-binding globulin (SHBG) levels, and hence lower free testosterone levels, include hyperthyroidism and human immunodeficiency virus infection [34].

10.4.2 Pelvic Floor Disorders

Disorders of the pelvic floor, including pelvic organ prolapse (POP) and stress urinary incontinence, affect approximately one-third of the female population today. There is conflicting evidence regarding the effect of POP on sexual function. Cross-sectional studies have shown that pelvic floor disorders, including POP, are associated with a large sexual dysfunction burden. Several studies have suggested that pain with sexual activity noted prior to surgery may be attributable to POP. Following surgical repair, most patients experience improvements in their sexual response. However, surgical approaches involving abdominal or transvaginal mesh may result in a decline in sexual function and worsening of dyspareunia [35]. On the other hand, sexual function in women with mild and moderate prolapses may improve with physical rehabilitation.

On the other hand, perineal tears may have a negative impact on female sexual function. Ahmed et al. [36] assessed women who had third- or fourth-degree perineal tears after vaginal delivery (study group), comparing them to women who underwent episiotomy or had minor lacerations (control group). After 12 months, and despite slight improvement, sexual function was significantly lower in those who had tears as compared to the control group. Women in the study group showed significant decreases in FSFI domain scores (desire, arousal, lubrication, orgasm, satisfaction, and pain) 12 months postdelivery [36].

10.4.3 Urinary Incontinence

Urinary incontinence may trigger problems that may contribute to FSD, namely, loss of urine during coitus (coitus incontinence), night losses associated to urgency, and fear of bedwetting [37]. Urinary incontinence related to coitus has been described in two ways: urinary incontinence associated to penetration and associated to orgasm ("squirting") [38]. Fear of malodorous and urinary incontinence during coitus has been associated with alteration of image and self-esteem and, thus, a decrease in sexual activity [39].

Urinary urgency symptoms, especially in the presence of mixed urinary incontinence (MUI), were associated with anxiety disturbances, mood disturbances (depression symptoms), and low quality of life related to stress urinary incontinence that ultimately affect sexual life. Altered sexual domains, as measured with the FSFI, may vary in accordance to the type of urinary incontinence: (1) urgency urinary incontinence may relate to a reduction of lubrication and increase of pain associated to sexual activity; (2) MUI has been related to a reduction of sexual satisfaction; (3) while stress urinary incontinence has no impact on sexual activity [40].

On the other hand, postmenopausal women with urinary incontinence had more severe vulvovaginal symptoms and vice versa [30]. Thus, 77.9% of women presented with at least one vulvovaginal symptom, being the three most prevalent complaints dryness, irritation, and itching. In this population, urinary incontinence of any degree was observed in 54.9%, with 42.6% being slight to moderate and 12.3% severe to very severe. These issues have a negative impact on emotional well-being and body self-image [41]. In addition, vulvar symptoms and diseases may associate with a higher risk for urinary incontinence and other urinary symptoms [42].

10.4.4 Endocrine Disorders

Overt or subclinical hypothyroidism and hyperthyroidism have been associated with reduced sexual desire [43]. Oppo et al. [44] reported that abnormal thyroid function (hypo- and hyperthyroidism) significantly impairs female sexual function, as assessed by the FSFI questionnaire, and that restoration to the euthyroid state is associated with a rapid improvement of most of its domain scores. In addition, biochemical restoration to euthyroidism was associated with normalization of desire, satisfaction, and pain domains, while arousal/lubrication and orgasm remained significantly different as compared to healthy euthyroid controls, in spite of some improvement of the orgasm [44]. Correction of hypothyroidism was associated with a normalization of desire, satisfaction, and pain, while arousal and orgasm remained unchanged. Treatment of hyperthyroid women normalized sexual desire, arousal/lubrication, satisfaction, and pain, while orgasm remained significantly unchanged. It seems that the risk of sexual dysfunction is higher among women with nodular goiter [45].

Polycystic ovary syndrome (PCOS) is often characterized by clinical and/or biochemical signs of hyperandrogenism, with or without oligo-anovulation or anovulation, or polycystic ovaries. Women with PCOS have psychological (feeling less

attractive, less feminine, more depressed) and biological (obesity and infertility) factors that may negatively influence their sexual desire [46]. They have worse sexual function, compromising arousal, lubrication, satisfaction, and more pain during the sexual intercourse, besides also having worse self-perception of their health condition than women with normal gonadal function. Obesity/overweight, clinical manifestation frequently associated to PCOS, negatively correlated to the several aspects of quality of life, significantly worsening physical/psychological relation with the environment and health aspects, but it did not correlate to female sexual function [47]. Infertility and alopecia were the most significant factors that contributed to a low FSFI score in women with PCOS, but other clinical characteristics such as hirsutism, acne, irregular menstruation, and android obesity (waist/hip ratio ≥0.8) were not statistically significantly associated with sexual function [48].

10.4.5 Depressive Symptoms

Depressive symptoms are more prevalent in women than in men, and peculiar hormone changes during reproductive years and menopause may contribute to this gender difference. However, differences in socialization, education, socioeconomic factors, discrimination, and male factors may contribute to the high rate observed during female second half of life. Women with climacteric symptoms, anxiety, perceived stress, and insomnia may also contribute to FSD associated with depressive symptoms [49]. The presence of depressive symptoms confers a 50–70% increased risk of sexual dysfunction, and the occurrence of the latter is associated with a 130–210% increased risk of depression [50]. Adding a layer of complexity, most antidepressants are associated with decreased sexual desire [51]. In the Hypoactive Sexual Desire Disorder Registry for Women study, 34% of a clinical sample of women with acquired, generalized HSDD were found to have concurrent depressive symptoms or were being treated with antidepressant medications. However, 58% of women had not been diagnosed or treated for depression before entering the study [52].

10.4.6 Cancer

The pathogenesis of sexual problems in female cancer patients is multifactorial, relating to medical, psychological, physiological, and sociological factors. Although sexual dysfunctions affecting women with cancer belong to the same categories as FSD seen in the general population, addressing sexual health issues in cancer patients still meets multiple barriers. Cancer or its treatment may bring many emotional and physical changes that induce women to feel less interested in sexual life. Therefore, patients with cancer are prone to neglect sexual life, with a negative impact on the relationships with their partners. Moreover, time constraints, reluctance of physicians in investigating this aspect, and embarrassment of women to ask about these problems may represent further difficulties in approaching sexual problems in cancer survivors.

Cancer by itself, as well as its treatment, may directly produce FSD [53]. Decreased sexual desire is a common issue for women after a diagnosis of breast cancer, ranging from 23 to 80% of women [54]. Sexual problems are independently associated with being postmenopausal (potentially provoked by chemotherapy), having vasomotor symptoms, and taking aromatase inhibitors [55]. Chemotherapy increases the likelihood of sexual complaints compared with surgery and/or radiation [56]. In addition, aromatase inhibitor therapy is associated with vaginal dryness, dyspareunia, and decreased sexual desire.

10.4.7 Medication-Induced Sexual Dysfunction

Chronic use of medication is frequent in postmenopausal women. The most frequently used medications are antidepressants and antihypertensive drugs. This circumstance has to be considered both in the diagnostic and in the therapeutic approach.

10.4.7.1 Antidepressants

Sexual dysfunction is commonly associated with depression. Due to this, it is important to assess possible sexual dysfunctions before and after starting antidepressant therapies [57].

Selective serotonergic reuptake inhibitors (SSRIs) are known to induce sexual side effects, having a negative impact on quality of life [51]. Sexual dysfunctions have also been observed, however, less frequently, with antidepressants that increase noradrenaline or dopamine uptake and the 5-HT2 receptor blockers [58]. It is advised to discuss with the patient these aspects and the possible influence that the use of antidepressants could have on her sexual life, sometimes having to switch from serotonergic reuptake inhibitors to other antidepressants [57].

SSRIs and serotonin-norepinephrine reuptake inhibitors are the most commonly prescribed antidepressants [59]. Possible sexual adverse effects of SSRIs are decreased desire, arousal difficulties, and delayed/absent orgasm. The reported incidence varies among studies and ranges from 30 to 70% [60]. Other medications must be considered as a possible source of sexual dysfunction in menopausal women. A detailed list is shown in Table 10.2.

Antidepressants known to cause sexual dysfunctions in more than 25% of users are fluoxetine, paroxetine, sertraline, venlafaxine, and citalopram [51]. They usually affect sexual desire, arousal, and orgasm. Antidepressants like bupropion, vilazodone, and nefazodone are known to have a low impact on sexual function affecting less than 5% of patients [57].

10.4.7.2 Antihypertensive Drugs

It is still not fully known if antihypertensive drugs are associated with sexual dysfunction in women. Hypertension, per se, is associated with sexual dysfunction. It is difficult to ascertain to what extent will the medication or the disease be responsible of the sexual dysfunction [61]. In men, antihypertensive drugs like beta-blockers and diuretics are known to induce sexual dysfunction [62].

Table 10.2 Medications associated with sexual dysfunction

Antidepressant/mood stabilizers
Selective serotonin reuptake inhibitors
Tricyclic antidepressants
Benzodiazepines
Lithium
Antipsychotics
Cardiovascular medications
Beta-blockers
Digoxin
Lipid lower medications
Other drugs
Oral contraceptives
Gonadotropin-releasing hormone agonist
Antiandrogens
Neuroleptic medications
Steroids
Antiepileptics
Antihistamines
Anticholinergics

Data from the Systolic Blood Pressure Intervention Trial with 690 women and 26.5% sexually active did not find differences in sexual activity among hypertense women using or not using antihypertensive drugs. However, the study found that women taking an angiotensin-converting enzyme inhibitor or angiotensin receptor blocker were more likely to be sexually active than women not using these medications [63]. Data from the National Social Life, Health, and Aging Project found that women using diuretics had a decreased sexual activity [62].

Although further investigation is warranted, considering what is known from men, and the available data related from women, angiotensin-converting enzyme inhibitor or angiotensin receptor blockers may be considered the antihypertensive drugs with less impact on women's sexual function.

10.5 General Management

After the menopause, the most common forms of sexual dysfunction are genitopelvic pain/penetration disorder, sexual interest/arousal disorder, and female orgasmic disorder [64]. Using a stepped care approach is recommended. The PLISSIT model (permission, limited information, specific suggestions, and intensive therapy) is still relevant and recommended to be followed when managing sexual dysfunction [65].

After the sexual interview, the patient's expectations must be assessed. This is useful for checking up on future progress. For many postmenopausal women, sexual intercourse can remain as the main target when seeking for help. Satisfactory sexual intercourse may be one of the goals in many cases. Another good option for checking progress is the use of validated questionnaires.

For the first two steps of the PLISSIT model (permission and limited information), the clinician must work mostly as an education provider [65]. As there is no standard in terms of sexuality, clinicians must avoid giving standard information and provide reassurance [66]. It is important evaluating all possible sexual issues before starting any treatment. Education about sexual anatomy, sexual physiology, and the changes that a woman may suffer after menopause can reduce anxiety and increase acceptance of the normal and pathological changes that may take place [11].

Patients have to be aware of the high prevalence of the GUSM and possible preventive strategies and treatments. It is also important to focus on education aimed at improving the quality of sexual relationship with her partner or partners. It is common that the partners of postmenopausal women may also suffer of chronic medical conditions limiting sexual interaction. If there is a physical limitation, sexual positions or the use of pillows can be taught as part of the specific suggestions [67, 68].

In the third step (specific suggestions), non-pharmacologic options should initially be offered. Non-pharmacologic options include counseling, couple therapy, pelvic physical therapy, psychotherapy, cognitive-behavioral therapy, privacy promotion, body image improvement, and the use of sexual devices. Education on moisturizers, lubricants, and sexual devices and on the possible need of longer foreplay should also be offered. Studies refer that more than 50% of patients describe their treatment as successful after sex therapy [69].

Sensate focus therapy is actually used in most of sexual dysfunctions after menopause. Patients are taught to perform graded series of sensual touching exercises. The objectives of sensate focus therapy are to improve intimacy and reduce sexual-related anxiety while restarting sexual activity gradually. Sensate focus therapy is known to have an important effect on sexual satisfaction and improve symptomatology [70].

When sexual dysfunction has been suffered for a long period, or is complicated with other comorbidities, education may not be enough, and a specialized sex therapy may be indicated, starting the last step (intensive therapy) [71].

10.5.1 Genito-Pelvic Pain/Penetration Disorder

The genito-pelvic pain/penetration disorder is defined when one of the following criteria is presented: pain experienced during attempted or as a result of vaginal penetration; pain, fear, or anxiety in anticipation to intercourse; and tensing of the pelvis in response to attempted penetration [9].

Genito-pelvic pain/penetration disorder is common among postmenopausal women. There are specific conditions in relation to climacteric that can lead to or worsen genito-pelvic pain/penetration disorder. These specific conditions are the GUSM, pelvic floor disorders, and pharmacology-related problems.

10.5.1.1 The Genitourinary Syndrome of Menopause

The GUSM is defined as the combination of signs and symptoms associated with estrogen deficiency that appear in the external genitals, pelvic floor, vagina, urethra, and bladder, which are generally associated to sexual dysfunction [72]. The term was intended to be more inclusive with other symptoms that are not limited to the

vulva and the vagina [73]. It is estimated that the GUSM is present in 50% of postmenopausal women, from 25% in perimenopausal women to 70% in women over 70 years [74]. However, appropriate treatment of different vulvovaginal and urinary complaints requires individual assessment of its components in order to provide a more successful treatment and results [75]. Despite the promotion of some "magic" (panacea) treatments for the syndrome, women still complain because some present a mix of clinical entities that do not respond to a single intervention.

As previously mentioned, low genital tract atrophy is highly prevalent in postmenopausal women, and symptoms' severity is progressive. Vaginal moisturizers and topical estrogen applications have been recommended for decades and still have a place, especially among young postmenopausal women [26]. However, their efficacy is reduced over time since menopause onset increases. A new approach to prevent and treat vulvovaginal atrophy could be based on the vaginal use of DHEA-S or prasterone. Several double-blind, placebo-controlled, randomized trials have shown that daily intravaginal 0.50% prasterone improves moderate to severe dyspareunia and dryness [76]. Oral use of ospemifene is also a good option for women who are not candidates or do not wish to use vaginal treatments [77].

10.5.1.2 Pelvic Floor Disorders

Pelvic organ prolapse or incontinence can be a physical impediment to sexual intercourse. In addition, prolapse and incontinence often lead to a deterioration of the body image and to the capacity of feeling sexually attractive [78]. Urinary and fecal incontinence, per se, can cause sexual dysfunction. These problems usually require surgery as a treatment, being sexual satisfaction after pelvic surgery influenced by the type of performed surgery [79]. Hysterectomy for organ prolapse has been reported as having a positive effect on sexual functioning [80]. Total vaginal meshes are associated with an increase in dyspareunia [81].

General recommendations for managing patients with pelvic floor disorder and sexual dysfunction are:

- Pelvic floor muscle training has demonstrated an improvement in desire, arousal, and orgasm and should be recommended [82].
- Weight control is recommended as an essential part of the specific suggestions. Increased BMI represents a risk factor for both urinary incontinence and sexual dysfunction [83].
- A careful individualized selection of patients and materials prior to any pelvic floor surgery or implantation of vaginal meshes is recommended [79].

10.5.2 Female Sexual Interest/Arousal Disorder

The female sexual interest/arousal disorder is defined by the presence of at least three of the following criteria: reduced/absent interest in sex, few erotic thoughts or fantasies, decreased start and rejection of sex, little pleasure during sex most of the time, decreased interest in sex even when exposed to erotic stimuli, and little genital or non-genital sensations during sex most of the time [9].

As defined in the DSM-4, the HSDD is currently part of the female sexual interest/arousal disorder. The loss of desire is estimated to affect more than 40% of all postmenopausal women, being the most common sexual disorder in this population [12, 84]. The management of the HSDD starts, as stated in the "general management" epigraph, with a stepped care approach. Simultaneously or if the non-pharmacological approach fails, there are specific pharmacological treatments for HSDD.

10.5.2.1 Hormone Therapy

Despite knowing that the level of circulating hormones poorly correlates with observed sexual function, hormone therapy has shown to improve sexual function in specific groups of postmenopausal women [85–87].

Estrogens have been suggested as a possible treatment for HSDD. Obtained evidence from the Women's Health Initiative shows that systemic estrogen did not improve sexual satisfaction or desire [88]. Testosterone has been studied and used for the HSDD. Due to adverse effects, most of the presentations are no longer available, and the use of testosterone is almost restricted to topical formulations. Common side effects related to the use of testosterone include decrease of high-density lipoproteins, hirsutism, acne, and virilizing changes with high dosages [89, 90]. However, the UK NICE Menopause Guideline recommends testosterone supplementation for menopausal women if hormone replacement therapy alone is not effective [91], but no pharmaceutical preparation has been approved in most countries.

Systemic DHEA failed at improving sexual desire in peri- and naturally postmenopausal women but was effective when used in women with adrenal insufficiency [92]. However, a more recent evidence from a meta-analysis suggests that DHEA-S supplementation may improve female sexual function, although with some androgenic side effects [93].

Tibolone has shown to improve sexual function and the satisfactory sexual event rate. In a randomized controlled trial, women using oral tibolone experienced a greater increase in the satisfactory sexual event rate and a reduction in sexuality-related personal distress, compared to the control group using estrogen plus norethisterone [94–96]. The oral use of ospemifene has shown to significantly increase total FSFI scores when compared to placebo, in the domains of sexual pain, arousal, and desire but only among women suffering of GUSM [77].

The use of vaginal DHEA for 12 weeks may improve four domains of sexual function and the desire domain as assessed with the Menopause Specific Quality of Life and Abbreviated Sex Function questionnaires in comparison to placebo. The arousal domain was improved by 68%, arousal/lubrication by 39%, orgasm by 75%, and dryness during rapport [97].

10.5.2.2 Central-Acting Agents

Flibanserin is the only drug in the USA approved by the Food and Drug Administration for female HSDD [98]. Flibanserin is a serotonin receptor 1A agonist/serotonin receptor 2A antagonist that causes a transient central decrease of serotonin and an increase of dopamine and norepinephrine in selected brain areas. Daily oral use of 100 mg of flibanserin at bedtime has shown to increase sexual

desire, improve the number of satisfactory sexual events, and reduce distress associated with low sexual desire in postmenopausal women [99, 100]. Most frequent adverse effects include dizziness, somnolence, nausea, fatigue, and hypotension making 8–13% of women discontinue the drug [101].

Bupropion is a commonly used antidepressant. Bupropion is a norepinephrine and dopamine reuptake inhibitor with no direct serotoninergic effect. In clinical trials bupropion has shown to improve sexual satisfaction, function, and desire in premenopausal women when compared to placebo [102].

Bremelanotide is a melanocortin 3 and 4 receptor agonist. In clinical trials bremelanotide has shown to increase the number of sexually satisfying events in premenopausal women [103]. No randomized controlled trials have been performed in postmenopausal women. Currently a subcutaneous formulation is being studied. It is administered 45 min before anticipated sexual activity.

10.5.2.3 Natural Remedies

Tribulus terrestris is an annual plant that might increase levels of bioavailable testosterone. It has been used in traditional Indian medicine for the improvement of sexual function. A randomized, placebo-controlled trial of 30 premenopausal women in each group showed an improvement in desire, arousal, lubrication, satisfaction, and pain domains of the FSFI [104].

Trigonella foenum-graecum is a traditional herbal drug and spice. In a randomized, placebo-controlled trial of 115 women (*Trigonella* $n = 59$ and placebo $n = 56$) experiencing menopausal symptoms, treatment with *Trigonella foenum-graecum* seed extract significantly improved sexual function [105].

10.5.3 Female Orgasmic Disorder

The female sexual orgasmic disorder is defined by reduced intensity, marked delay, infrequency, or absence of orgasm [9]. The female orgasmic disorder is commonly associated with female sexual interest/arousal disorder; due to this, most of the treatments described for female sexual interest/arousal disorder are useful when treating patients affected with female orgasmic disorder. Specific treatments for the female orgasmic disorder include directed masturbation, coital alignment, sexual enhancement products, and specific pharmacological treatments such as phosphodiesterase type 5 inhibitors and oxytocin.

Masturbation training consists of gradual series of exercises starting with genital auto-exploration, followed by arousal stimuli and ending in masturbation to orgasm (normally in 10–11 sessions) [106]. Various trials have evaluated masturbation training, showing that it increases orgasm consistency, sexual self-acceptance, and sexual pleasure [107].

The coital alignment technique helps improving the frequency of orgasms when having intercourse with a male partner. The coital alignment technique is a variant of the missionary position. The male partner lies above the woman and moves upward until the dorsal side of his penis presses against the clitoris [108].

Improvement in orgasm consistency and sexual pleasure has been observed after using the coital alignment technique [108, 109].

Vibrators and sexually explicit media are often used in masturbation training when enhancing sexual stimulation is needed. Vibrators produce a different orgasmic pattern; they allow more frequent and faster orgasms. It must be taken into consideration that some women may not consider a faster orgasm a better orgasm [110]. Considering that postmenopausal women may not know much about different sizes and types of vibrators and dildos, there is a need for attending physicians to know about the different sizes and materials [111]. Some products may be comfortable for vaginal or anal insertion, but others can cause genital trauma.

Phosphodiesterase type 5 inhibitors have some benefits on arousal and orgasmic function. These drugs work augmenting genital blood flow through the guanosine monophosphate and nitric oxide system. Most studies regarding phosphodiesterase type 5 inhibitor use do not show a clear clinical improvement in women. Phosphodiesterase type 5 inhibitors do not act on central mechanisms associated with subjective sexual experience; this may be the reason why there is no evidence of improvement on women's sexual subjective experience [112].

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