

Assessment of female sexual dysfunction: review of validated methods

Raymond C. Rosen, Ph.D.

Department of Psychiatry, UMDNJ-Robert Wood Johnson Medical School, Piscataway, New Jersey

Objective: To review validated methods for the assessment of female sexual function in clinical trials.

Design: Evaluation of recent peer-review literature on sexual function assessment in women.

Setting: International conference on androgen insufficiency in women.

Patient(s): Women with sexual dysfunction due to androgen insufficiency or other causes.

Intervention(s): None.

Main Outcome Measure(s): Measures of sexual function in women.

Result(s): Design and measurement problems in the assessment of sexual functioning in women have limited clinical trials in female sexual dysfunction. Objective measures, such as vaginal photoplethysmography or Duplex ultrasound, have been used in some studies but lack standardization and are unsuitable for use in large-scale clinical trials. A variety of interview methods, validated questionnaires, and event log measures have been used for assessing sexual function in recent trials of androgen replacement therapy. Each of these methods has distinct advantages and disadvantages, although validated questionnaires have provided the most reliable findings to date. Recent Food and Drug Administration guidelines on assessment of female sexual function in clinical trials are critically reviewed.

Conclusion(s): Despite their prevalence and clinical significance, sexual problems in women have often been neglected in clinical trials. A major obstacle in the design of clinical trials in this area has been the need for sensitive and reliable measures of outcome. Of the currently available measures, self-reported event logs or questionnaires are best suited for research or clinical assessment of female sexual function. (Fertil Steril® 2002;77(Suppl 4):S89–93. ©2002 by American Society for Reproductive Medicine.)

Key Words: Female sexual dysfunction, measurement and assessment, sexual arousal, vaginal photoplethysmography, questionnaires, event logs, personal distress, quality of life

Sexual problems in women are highly prevalent and are frequently associated with personal distress and impaired quality of life. In the National Health and Social Life Survey (1), a large epidemiological study of 1,622 women between the ages of 18 and 59, a strong association was found between problems of sexual desire, arousal, and pain with decreased physical satisfaction, emotional satisfaction, and overall life satisfaction. Arousal disorders in women, in particular, were strongly predictive of diminished relationship satisfaction and overall life satisfaction. Both psychosocial stresses and physical health problems were associated with the development of sexual difficulties in this study. Overall, approximately 42% of women complained of one or more sexual problems, compared with about 30% of men. Similar results have been obtained in studies of sexual function in postmenopausal women (2–4).

Androgen deficiency in women has been associated with an increased rate of sexual problems or complaints in a number of studies (5–9). These problems are frequently encountered in oophorectomized women and those with androgen deficiency from other causes (7, 8). Among the most commonly reported problems are decreased sexual desire or libido, lack of responsiveness to sexual stimulation, and diminished sexual pleasure or satisfaction. Problems of arousal/lubrication and orgasm are less commonly reported, although the specific sexual difficulties and means of assessment have varied widely from one study to another. As noted by Bancroft (10), assessment of sexual function in women with low androgen is frequently confounded by the effects of depressed mood or other comorbid medical or psychiatric disorders. Premorbid sexual functioning is typically not assessed, and the effects

Received October 16, 2001; revised and accepted January 8, 2002.

Reprint requests: Raymond C. Rosen, Ph.D., Department of Psychiatry, UMDNJ-Robert Wood Johnson Medical School, 675 Hoes Lane, Piscataway, NJ 08854 (FAX: 732-235-5818; E-mail: rosen@umdnj.edu).

0015-0282/02/\$22.00
PII S0015-0282(02)02966-7

of treatment may be confounded by pharmacological effects of supraphysiological T administration. Despite these limitations, recent studies have strongly implicated the role of androgen deficiency in female sexual dysfunction (5–7).

Measurement approaches for male and female sexual dysfunction have proliferated in recent years, spurred in large part by the development of new treatments for male and female dysfunction. In the past, physiological measures of penile tumescence and rigidity in males and vaginal blood flow in females played an important role in clinical and research studies. Despite their potential precision and objectivity, these measures have not been predictive of subjective arousal in women (11, 12). More recently, a variety of brief, self-report measures have been developed for assessing male and female function across a variety of sexual domains (e.g., desire, arousal, orgasm, satisfaction). These brief, self-report measures have been shown to have a high degree of reliability and validity and to be sensitive to treatment interventions. Accordingly, they are widely employed in clinical trials. Daily diary or sexual event logs have similarly been developed for this purpose.

Although female sexual disorders have been less studied overall than male disorders, efforts are underway to refine the diagnosis and classification of these disorders (13). An important contributing factor to this field has been the development of validated instruments for the assessment of sexual function. These instruments have been used as primary endpoints in clinical trials, as well as for clinical screening and diagnostic purposes. Finally, few instruments have been developed for assessment of life satisfaction or quality of life changes associated with sexual dysfunction.

MEASUREMENT APPROACHES

Objective Measures

In women, the most widely used physiological method for assessing sexual response is the vaginal photoplethysmograph (12, 13). The vaginal photoplethysmograph consists of a light-emitting diode and sensitive photocell detector enclosed in a tampon-sized, clear acrylic probe. The signal obtained reflects changes in the amount of light back-scattered to the photocell from the surrounding vasculature and provides a sensitive, albeit indirect, measure of vaginal vasoengorgement. Depending on the mode of recording, measures of vaginal blood volume or vaginal pulse amplitude (VPA) can be obtained. VPA is regarded as the more sensitive and reliable measure (12) and is more generally used in studies of treatment outcome. Although this method has been used in a variety of research settings, the method is not well standardized and there is no clinical application of the procedure to date. Other methods for assessing female genital vasocongestion, such as labial temperature or clitoral blood flow measures, Doppler ultrasonography (14), and magnetic resonance imaging (15), have recently been reported, al-

though none are widely used at present. At least one study has demonstrated the effects of androgen deficiency on VPA in postmenopausal women (16).

Self-Report Measures

Self-report or questionnaire methods have significant advantages in a number of areas. These methods are well standardized, relatively unobtrusive and inexpensive, and easy to administer and score, and normative values are available in both clinical and nonclinical populations. However, differences in educational, ethnic, or cultural background may influence the validity of these tests. Self-report measures of sexual function exist in several forms, including self-administered questionnaires, daily diary records, and event log measures of sexual behavior. Self-administered questionnaires have a long history of use in psychological and sociological studies of sexual behavior. The Derogatis Sexual Function Inventory, for example, is a 245-item, multidimensional scale that assesses a broad range of sexual behaviors in 10 separate domains (17). Despite its strong psychometric properties, the instrument is not widely used in clinical trials because of its excessive length and complexity. Instead, a number of brief sexual function scales have been developed in the past decade, which are more suitable for use in trials of male or female sexual dysfunction. The following questionnaires have recently been developed and are particularly recommended for trials of female sexual dysfunction.

Brief Sexual Function Index for Women (BSFI-W)

This is a 22-item, multidimensional self-report instrument for women that assesses sexual function in seven dimensions: sexual thoughts/desires, arousal, frequency of activity, receptivity/initiation, pleasure/orgasm, relationship satisfaction, and sexual problems. The scale also yields an overall composite score. The measure was originally validated in a nonclinical sample of 225 women ages 22–55 years, 187 of whom had regular sexual partners (18). Significant differences were observed on most dimensions of sexual function between women with and without sexual partners. More recently, the scores of the original validation sample were compared with a clinical sample of 104 women in the same age range who had undergone bilateral oophorectomy and hysterectomy (19). This study demonstrated significantly lower scores on six of seven dimensions of sexual function and the overall composite scores of oophorectomized women compared with controls. In particular, the dimensions of sexual desire, arousal, and frequency of activity were the most significantly different between the two groups. Most recently, this measure was found to be responsive to T replacement therapy effects in the sample of women with bilateral oophorectomy (20).

Female Sexual Function Index (FSFI)

This is a recently developed, brief (19-item) self-report questionnaire that assesses sexual functioning in women in

six separate dimensions (desire, arousal, lubrication, orgasm, satisfaction, pain) (21). In addition, a total scale score can be computed according to a simple scoring algorithm. The questionnaire was developed for use in clinical trials of female sexual dysfunction and was validated in a multicenter study of women with sexual arousal disorder ($n = 128$) and age-matched controls ($n = 131$). The measure was shown to have a high degree of internal consistency and test-retest reliability and differentiated well between the two groups. Highly significant differences were observed in all six dimensions between the patients and controls, indicating that the measure is very sensitive in differentiating responses between sexually dysfunctional and nondysfunctional women. The FSFI is relatively easy to administer and score and is currently being used in a number of clinical trials of female sexual dysfunction. The treatment responsiveness of the measure is uncertain.

Sexual Function Questionnaire (SFQ)

The SFQ is a 31-item, multidimensional questionnaire recently developed for use in clinical trials of sildenafil in women with sexual arousal disorders (22). The questionnaire assesses sexual function in seven dimensions: desire, physical arousal, lubrication, enjoyment, orgasm, pain, and partner satisfaction. The questionnaire was validated in two, large-scale clinical trials including 781 women with sexual dysfunction. A control sample of 201 women without sexual dysfunction was used for comparison purposes. Highly significant differences were found between the patient and control groups on each of the dimension scores ($P < .0001$), and the questionnaire showed strong internal consistency and test-retest reliability. Treatment responsiveness (sensitivity) was also demonstrated, as significant changes were noted at the end of treatment in each of the dimensions for women who reported improvement versus those who did not improve with treatment ($P < .001$). Although somewhat lengthier than the previous two instruments, the SFQ has strong psychometric properties and initial validation data. The high level of treatment responsiveness suggests that the measure is well suited for use in clinical trials of androgen replacement therapy or other treatment interventions.

Daily Diaries and Event Logs

Daily diaries or sexual event logs are brief, self-report instruments that are often used to obtain frequency data in clinical trials. These measures have been used extensively in clinical trials of male sexual dysfunction and are favored by regulatory agencies as primary endpoints for trials of male or female dysfunction. Event logs or daily diaries for men typically include assessment of variables such as intercourse frequency and satisfaction, quality of erection, and medication use. Diaries typically require the subject to record sexual activity on a daily basis, whereas event logs are completed only on days that sexual activity occurs. For example, the Sexual Encounter Profile is a six-item event log that has been

used in several multicenter, clinical trials of erectile dysfunction. A corresponding version for women (Sexual Encounter Profile for Women) has been developed for use in clinical trials of female sexual dysfunction. Other event log or diary measures are available, although published data on these instruments are not available. For example, the Female Intervention Efficacy Index assesses immediate response to treatment and has been used in recent clinical trials, although validation data on the instrument have not been published to date.

The potential advantage of diary or event log measures is their ability to provide quantitative data regarding the frequency of sexual activity and proportion of successful attempts at intercourse or other forms of sexual activity. However, event logs or diaries are highly restricted in the scope of measurement and do not provide the broad, multidimensional assessment of response afforded by self-administered questionnaires. Since these measures are typically completed at home, they are also susceptible to various forms of response bias or error. Finally, these measures may not be suitable for assessing subjective aspects of female sexual response, such as desire or subjective arousal. These latter domains are essential to address in clinical trials of androgen replacement therapy in women.

Structured Interviews

Structured interview approaches, such as the Structured Diagnostic Interview, are widely used in psychiatric outcome studies. These approaches have been less frequently used in sexual function assessment studies. The Derogatis Sexual Function Interview is based on an earlier questionnaire measure developed by the same author (23) and is available for use in clinical trials of male and female dysfunction. Although the structured interview approach offers potential advantages in terms of breadth of assessment and clinical validation, the method has yet to be evaluated in large-scale clinical trials.

Personal Distress and Quality of Life

To qualify for the diagnosis of sexual dysfunction, a woman should show evidence of significant personal distress in relation to her sexual problem (11). Personal distress can be assessed by means of interview or questionnaire. The Female Sexual Distress Scale is a 12-item scale that assesses subjective distress associated with sexual dysfunction in women. The instrument has been evaluated in several recent clinical trials (24) and has been shown to have a high degree of test-retest reliability (0.91) and internal consistency (0.88). The measure also discriminates well between women with and without sexual dysfunction and has been shown to be sensitive to the effects of treatment. The measure is highly recommended for inclusion in future clinical trials of female sexual dysfunction.

In contrast, few quality of life measures have been developed specifically for use in clinical trials of sexual dysfunction.

tion in men or women. The Psychological General Well-Being Index was used to evaluate quality of life changes in the recent study of androgen replacement in oophorectomized women (20). Recently, Fugl-Meyer et al. (25) have developed a brief, eight-item life satisfaction checklist for quality of life assessment in sexual dysfunction trials. This measure includes single-item scales for assessment of overall life satisfaction, sexual life satisfaction, interpersonal function, family life, leisure, work, and recreation. The measure was developed primarily for use in trials of male erectile dysfunction and has not been independently validated in trials of female sexual dysfunction. Clearly, this is an important area for future research.

A guidance document on female sexual dysfunction was issued by the Center for Drug Evaluation and Research, a branch of the Food and Drug Administration (FDA), in May 2000 (26). This document outlines the FDA's recommendations for the conduct of clinical trials in female sexual dysfunction (FSD). FSD by definition comprises one or more of four essential components: decreased sexual desire, decreased sexual arousal, dyspareunia, and orgasmic dysfunction. The definition of sexual dysfunction should also include a measure of personal distress. According to the document, personal distress should reflect a degree of psychological dissatisfaction with sexual functioning in the affected woman. This is an important inclusion criterion for clinical trials of FSD.

Appropriate study populations are defined and include premenopausal women, naturally postmenopausal women, surgically menopausal women, and women taking oral contraceptives or hormone replacement therapy. Women with significant comorbid illnesses or those taking medications that might directly affect sexuality or having other potential confounding factors (e.g., partner dysfunction) should be excluded from clinical trials when possible.

The FDA guidance document recognizes the value of questionnaires and self-report measures in the assessment of female sexual function. However, emphasis is placed on the need for separate validation of these measures before their use in clinical trials. Regarding selection of endpoints for clinical trials of FSD, the FDA document makes the following specific recommendation: "These endpoints should be based on the number of successful and satisfactory sexual events or encounters over time. The determination of successful and satisfactory should be made by the woman participating in the trial, as opposed to her partner" (26).

The document further defines such events or encounters as including sexual intercourse (with or without orgasm), oral sex resulting in orgasm, or manual stimulation by self or partner resulting in orgasm. These events or encounters are typically recorded in daily records or event logs. Changes in the frequency of occurrence of these events before and after treatment should be compared in placebo-controlled trials with any new treatment agent.

Physiological measures, such as vaginal blood flow or clitoral engorgement, should be closely linked to the occurrence of successful and satisfying sexual events as defined above. The potential value of self-administered questionnaire scales as primary endpoints in clinical trials is not specifically addressed by the document, although the same reservations would presumably apply. Overall, the document is highly specific in recommending the use of frequency-based measures of successful sexual encounters, such as diaries or event logs, as primary endpoints in clinical trials of FSD.

This emphasis on frequency-based measures is controversial at present. In the recent trial of androgen replacement in oophorectomized women (20), for example, the BSFI-W questionnaire was found to be sensitive to androgen replacement effects in older, oophorectomized women, whereas a telephone diary measure was not. The selection of event log measures of sexual encounters as primary endpoints has a strong parallel in the recent clinical trials of male erectile dysfunction. Whereas this approach might be well suited for recording erections firm enough for intercourse, it may not be appropriate for measuring continuous or subjective variables that frequently characterize FSD. Questionnaire measures such as those described above may be more suitable for this purpose. Hopefully, this issue will be resolved as further clinical trial data become available.

Quality of life and personal distress measures are recognized as potentially valuable secondary outcomes. However, these should not be used as primary endpoints in clinical trials of FSD.

While recognizing the potential impact of sexual dysfunction in women and the need for further clinical trials, the FDA guidance document places constraints on the selection of patients and endpoints for study. In particular, these endpoints may not be ideally suited for the assessment of sexual function outcomes associated with hormone replacement therapy in women with androgen insufficiency.

SUMMARY AND CONCLUSIONS

A variety of measurement approaches are available for assessing FSD. Although physiological measures, such as vaginal photoplethysmography, are available, these are not suitable for use in large-scale clinical trials. Rather, a number of self-report and diary-based measures have been developed for multidimensional assessment of sexual function. Several of these measures have demonstrated adequate psychometric properties, including test-retest reliability, internal consistency, and discriminant validity. Only one structured interview method has been described in the literature thus far, and this method has not been widely used to date. Personal distress is an important component of FSD and can be reliably assessed by the Female Sexual Distress Scale. The FDA guidance document emphasizes the need for fre-

quency-based measures of successful sexual encounters as primary endpoints in clinical trials of FSD. This emphasis is controversial at present and may be modified as increasing data become available from clinical trials of hormone replacement therapy. Quality of life and personal distress measures are important secondary outcomes in studies of FSD.

References

1. Lauman EO, Paik A, Rosen RC. Sexual dysfunction in the United States: prevalence and predictors. *JAMA* 1999;281(6):537-44.
2. Bachmann GA, Leiblum SR, Kemman E, Colburn DW. Sexual expression and its determinants in the post-menopausal woman. *Maturitas* 1984;6:19-29.
3. Dennerstien L, Dudley E, Hopper J, Burger H. Sexuality, hormones and the menopausal transition. *Maturitas* 1997;26:83-93.
4. Rosen RC, Taylor JF, Leiblum SR, Bachmann GA. Prevalence of sexual dysfunction in women: results of a survey study of 329 women in an outpatient gynecological clinic. *J Sex Marital Therapy* 1993;(19):171-88.
5. Sherwin BB, Gelfand MM. The role of androgen in the maintenance of sexual functioning in oophorectomized women. *Psychosom Med* 1987;49:397-409.
6. Bancroft J. Androgens and sexual function in men and women. In: Bremner WJ, Bagatell C, eds. *Androgens in health and disease*. Totowa, NJ: Humana Press (in press).
7. Davis S, Tran J. Testosterone influences libido and well being in women. *Trends Endocrinol Metab* 2001;12:33-7.
8. Hulter B, Lundberg PO. Sexual function in women with hypothalamic-pituitary disorders. *Arch Sex Behav* 1994;23(2):171-83.
9. Cawood EH, Bancroft J. Steroid hormones, the menopause, sexuality and well-being of women. *Psycholog Med* 1996;26:925-36.
10. Bancroft J. Sexual effects of androgens in women. *Fertil Steril* 2002;77(Suppl 4):S55-9.
11. Laan E, Everaerd W. Physiological measures of vaginal vasocongestion. *Intl J Impot Res* 1998;10(Suppl 2):S107-10.
12. Rosen RC, Beck JG. *Patterns of sexual arousal: psychophysiological processes and clinical applications*. New York: Guilford Press, 1988.
13. Basson R, Berman J, Burnett A, Derogatis L, Ferguson D, Fourcroy J, et al. Report on the international consensus development conference on female sexual dysfunction: definitions and classifications. *J Urology* 2000;163:888-93.
14. Goldstein R, Berman JR. Vasculogenic female sexual dysfunction: vaginal engorgement and clitoral insufficiency syndrome. *Intl J Impot Res* 1998;10(Suppl 2):S84-90.
15. Heiman JR. Vaginal photoplethysmography and pelvic imaging: a comparison of measures. In: Program and abstracts of the 3rd Annual Female Sexual Function Forum, Boston, MA, 2001:167.
16. Tuiten A, Laan E, Panhuysen G, Everaerd W, Vroon P. Discrepancies between genital responses and subjective sexual function during testosterone substitution in women with hypothalamic amenorrhea. *Psychosom Med* 1996;58:234-41.
17. Derogatis LR, Melisaratos N. The DSFI: a multidimensional measure of sexual functioning. *J Sex Mar Ther* 1979;5:244-81.
18. Taylor JE, Rosen RC, Leiblum SR. Self-report assessment of female sexual function: psychometric evaluation of the Brief Index of Sexual Functioning for Women (BISF-W). *Arch Sex Behav* 1994;23:627-43.
19. Mazer NA, Leiblum SR, Rosen RC. The Brief Index of Sexual Functioning for Women (BISF-W): a new scoring algorithm and comparison of normative and surgically menopausal populations. *Menopause* 2000;7:350-63.
20. Shiffren JL, Braunstein GD, Simon JA, Casson PR, Buster JE, Redmond GP, et al. Transdermal testosterone treatment in women with impaired sexual function after oophorectomy. *N Engl J Med* 2000;342:682-8.
21. Rosen RC, Brown C, Heiman J, Leiblum S, Meston C, Shabsigh R, et al. The Female Sexual Function Index (FSFI): a multidimensional self-report instrument for the assessment of female sexual function. *J Sex Mar Ther* 2000;26:191-208.
22. Quirk FH, Heiman J, Rosen R, Laan E, Smith M, Boolell M. Development of a sexual function questionnaire for clinical trials of female sexual dysfunction. *J Women's Health Gender-Based Med* (in press).
23. Derogatis LR. The Derogatis Interview for Sexual Functioning (DISF/DISF-R): an introductory report. *J Sex Mar Ther* 1997;23:291-6.
24. Derogatis LR, Burnett A, Heiman J, Leiblum S, Rosen R. Development and continuing validation of the Female Sexual Distress Scale (FSDS). To be presented at the 4th Annual Female Sexual Function Forum, Boston, MA (October 29, 2001).
25. Fugl-Meyer AR, Lodnert G, Branholm I-B, Fugl-Meyer KS. On life satisfaction in male erectile dysfunction. *Intl J Impot Res* 1997;9:141-8.
26. Center for Drug Evaluation and Research. *Female sexual dysfunction: clinical development of drug products for treatment*. Rockville, MD: US Department of Health and Human Services, May 2000.