Sexual function in young women with spontaneous 46,XX primary ovarian insufficiency

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Objective: To assess sexual function in women with spontaneous 46,XX primary ovarian insufficiency after at least 3 months of a standardized hormone replacement regimen.
Design: Cross-sectional cohort, controlled.
Setting: National Institutes of Health Clinical Research Center.
Patient(s): Women with primary ovarian insufficiency (n = 143) and regularly menstruating controls (n = 70).
Intervention(s): Self-administered questionnaires, 100 μg/day E_2 patch, oral medroxyprogesterone acetate 10 mg for 12 days each month for patients.
Main Outcome Measure(s): Derogatis Interview for Sexual Function Self-Report (DISF-SR).
Result(s): Women with primary ovarian insufficiency had significantly lower DISF-SR composite scores compared with control women. Their serum total testosterone levels were significantly correlated with DISF-SR composite score, although this accounted for only 4% of the variance in this measure. Patients with testosterone levels below normal tended to have lower DISF-SR composite scores. Of patients with primary ovarian insufficiency, 9 of 127 (7%) scored below the second percentile on the composite sexual function score, compared with 1 of 49 control women (2%).
Conclusion(s): As assessed by the DISF-SR, sexual function is in the normal range for most young women with 46,XX spontaneous primary ovarian insufficiency who are receiving physiologic E_2 replacement. However, as a group, these young women score significantly lower on this sexual function scale than control women. (Fertil Steril® 2008;90:1805–11. ©2008 by American Society for Reproductive Medicine.)

Key Words: Sexual function, primary ovarian insufficiency, premature ovarian failure, premature menopause, primary hypogonadism, hypergonadotropic hypogonadism, hypergonadotropic amenorrhea, hormone replacement therapy, estrogen, testosterone

Premature ovarian failure, previously known as premature menopause, has been defined as the development of hypergonadotropic hypogonadism before the age of 40 years, which is two standard deviations below the mean age of natural menopause (1–3). This condition is associated with amenorrhea, symptoms of estrogen deficiency, and gonadotropin levels in the menopausal range. The prevalence is approximately 1 in 250 by age 35 and 1 in 100 by age 40 (4).

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The term "premature ovarian failure" is problematic, because it implies permanent cessation of ovarian function. In fact, many women with this condition experience intermittent ovarian function that may last for decades. Pregnancy may occur in some women many years after the diagnosis (5). Our preferred term for the condition is "primary ovarian insufficiency" as first introduced by Fuller Albright et al. in 1942 (6).

Sexual dysfunction can have harmful effects on relationships, self-esteem, and quality of life, yet sexual dysfunction commonly receives little attention in clinical practice. Sexual dysfunction in women involves the interaction of emotional, cultural, personal, interpersonal, contextual, and medical factors (7–10). In one national survey, approximately 25% of women reported marked distress about their sexual relationship and/or their own sexuality (7). The study found that the best predictors of sexual distress were markers of general

emotional well-being and emotional relationship with the partner during sexual activity. Physical aspects of sexual response in women, including arousal, vaginal lubrication, and orgasm, were poor predictors (7).

Young women find the diagnosis of spontaneous 46,XX primary ovarian insufficiency particularly traumatic (11). Disorders of mental health, especially depression, frequently underlie the presentation of sexual dysfunction (12). The traditional separatist notion that sexual dysfunction has either psychologic or organic origins has been replaced by an understanding that the two are closely linked and must be taken into consideration together (13).

There is little evidence specifically analyzing the relationship between sexual dysfunction and spontaneous 46,XX primary ovarian insufficiency (14). To our knowledge no controlled studies to date have specifically evaluated sexual function in women with this condition. We undertook the present study to determine if women who have spontaneous 46,XX primary ovarian insufficiency and are E_2 replete have sexual dysfunction compared with young women of similar age who have normal ovarian function.

SUBJECTS AND METHODS

Study Population

The study was approved by the Institutional Review Board of the National Institute of Child Health and Human Development, National Institutes of Health (Bethesda, MD). All women provided written informed consent. We recruited women with spontaneous 46,XX primary ovarian insufficiency by the internet and by clinician referral. We recruited control subjects by local advertisement.

From January 2000 to November 2005 we recruited 143 women with spontaneous 46,XX primary ovarian insufficiency and 70 control women of similar age who had normal ovarian function. We recruited patients and control subjects as part of a screening process for enrollment in a 3-year prospective double-blind randomized placebo-controlled trial to evaluate the effect of transdermal E_2/T therapy on bone density). The 3-year study was conducted under a cooperative research and development agreement between the National Institutes of Health and Procter and Gamble Pharmaceuticals (Mason, OH). To obtain a representative spectrum of sexual function in this population there was no a priori requirement that patients or controls have a sexual partner or be sexually active (13). No reference to sexual function was made as part of recruitment efforts.

Study Design

This was a controlled cross-sectional study designed to compare sexual function of women with spontaneous 46,XX primary ovarian insufficiency who receive a standardized hormone regimen for at least 3 months and women of similar age who have normal ovarian function. Women with spontaneous primary ovarian insufficiency were seen for two visits: 1) a baseline screening evaluation, at which time they had been off any estrogen/progestogen hormone therapy for at least 2 weeks; and 2) after receiving a standardized hormone regimen for at least 3 months consisting of a 100 μg E_2 patch and cyclic oral medroxyprogesterone acetate (10 mg for 12 days each month).

Women With Primary Ovarian Insufficiency

To be eligible for the study, patients had to meet the following inclusion criteria: 1) diagnosis of spontaneous 46,XX primary ovarian insufficiency before the age of 40 years (i.e., at least 4 months of oligo/amenorrhea and two FSH levels in the menopausal range, as defined by the local assay used and confirmed on two separate occasions at least 1 month apart); 2) age between 18 and 42 years; 3) no iatrogenic cause of the ovarian insufficiency or known chromosomal abnormality; 4) normal thyroid and adrenal function; and 5) no contraindication for hormone therapy. Screening baseline evaluation was as previously described (15).

Control Subjects

Control women were healthy, nonpregnant, and regularly menstruating (cycles between 21 and 35 days). They did not smoke more than 2 cigarettes per day or use alcohol ($<$2 drinks a day). They were taking no chronic medications and were not using hormonal contraception. They were compensated according to NIH guidelines.

Evaluation of Sexual Function

We used a self-report questionnaire; the Derogatis Interview for Sexual Function (DISF-SR—Female Version) is a reliable and well validated measure of sexual functioning designed for use in women (16). The DISF-SR has five domain scores: Cognition/Fantasy, Sexual Arousal, Sexual Behavior/Experiences, Orgasm, and Drive & Relationship. In addition there is the composite score, which is computed and summarizes sexual functioning across the five primary DISF-SR domains. The DISF-SR consists of 25 items measuring level of sexual activity and overall sexual functioning during the past 30 days. A combination of 9-point frequency scales (e.g., 0 = not at all and 8 = four or more times per day) and 4-point frequency scales (e.g., 0 = not at all and 4 = extremely) are used.

Assessment of each domain is computed as a scale score in terms of area T-score (generated through a normalizing transformation); a T-score of 50 places the respondent in the 50th percentile of the norm, a T-score of 30 places the respondent in the second percentile, and a T-score of 70 places her in the 98th percentile (16). Sexual function was evaluated in patients during the E_2-only phase of the hormone replacement cycle (not on progestin). In control women this was evaluated during the midfollicular phase of their menstrual cycle (days 5–12).

Hormonal Assays

Serum total T, free T, and E_2 were measured as previously reported (17). We measured serum total T by radioimmunoassay after extraction chromatography (Esoterix Endocrinology, Calabassa Hills, CA) (18). We determined serum free