ORIGINAL RESEARCH—ENDOCRINOLOGY

Is There a Correlation Between Androgens and Sexual Desire in Women?

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ABSTRACT

Introduction. For women, the correlation between circulating androgens and sexual desire is inconclusive. Substitution with androgens at physiological levels improves sexual function in women who experience decreased sexual desire and androgen deficiency from surgical menopause, pituitary disease, and age-related decline in androgen production in the ovaries. Measuring bioactive testosterone is difficult and new methods have been proposed, including measuring the primary androgen metabolite androsterone glucuronide (ADT-G).

Aim. The aim of this study was to investigate a possible correlation between serum levels of androgens and sexual desire in women and whether the level of ADT-G is better correlated than the level of circulating androgens with sexual desire.

Methods. This was a cross-sectional study including 560 healthy women aged 19–65 years divided into three age groups. Correlations were considered to be statistically significant at $P < 0.05$.

Main Outcome Measure. Sexual desire was determined as the total score of the sexual desire domain of the Female Sexual Function Index. Total testosterone (TT), calculated free testosterone (FT), androstenedione, dehydroepiandrosterone sulfate (DHEAS), and ADT-G were analyzed using mass spectrometry.

Results. Sexual desire correlated overall with FT and androstenedione in the total cohort of women. In a subgroup of women aged 25–44 years with no use of systemic hormonal contraception, sexual desire correlated with TT, FT, androstenedione, and DHEAS. In women aged 45–65 years, androstenedione correlated with sexual desire. No correlations between ADT-G and sexual desire were identified.

Conclusions. In the present study, FT and androstenedione were statistically significantly correlated with sexual desire in the total cohort of women. ADT-G did not correlate more strongly than circulating androgens with sexual desire and is therefore not superior to measuring circulating androgens by mass spectrometry. **Wåhlin-Jacobsen S, Pedersen AT, Kristensen E, Læssøe NC, Lundqvist M, Cohen AS, Hougaard DM, and Giraldi A. Is there a correlation between androgens and sexual desire in women? J Sex Med 2015;12:358–373.**

Key Words. Sexual Desire; Androsterone Glucuronide; Androgen Metabolites; Androgen; Testosterone; Androstenedione; DHEAS; 17b-Hydroxysteroid Dehydrogenase; FSFI; Woman

Introduction

Women's sexuality is influenced by various biological, psychological, and social factors. Lack of sexual desire includes hypoactive sexual desire disorder (HSDD) [1]. A Danish study of a nationally representative population found that sexual desire decreases with age and that the percentage of women aged 16–66 years who report rarely or never experiencing sexual desire ranges

from 10% in women aged 16–44 years to 20% in women aged 45–66 years [2]. Other factors associated with low sexual desire in women include being unmarried, low educational level and socioeconomic status, emotional problems, stress and depression, poor self-rated health, diabetes, or neurological disorders [2]. Several factors may underlie the association of age with sexual desire, such as an age-related decline in serum levels of estrogens and androgens and the various life stages women may experience: being single, seeking a partner, being in love, having children, developing cancer, having a chronic disorder, experiencing the psychological effects of menopause, partner sexual dysfunction, and losing a partner [1].

Low sexual desire is the most frequently reported sexual problem in women globally [3]. A study of 31,581 U.S. women found an increasing prevalence of low sexual desire from 17.8% in women aged 25–34 years up to 85.8% of women aged 75 and older. The prevalence of women reporting concurrent sexually related personal distress was highest (12.4%) in women aged 45–54 years [4].

Among the biological factors that influence women's sexual desire and the prevalence of HSDD, special attention has been given to the role of testosterone [5], which has been investigated in several studies with inconclusive results. In several larger interventional studies, testosterone therapy alone or in addition to postmenopausal hormone therapy (HT) has shown a beneficial effect on sexual function in women with HSDD after surgical [6–10] and natural menopause [11–15] and in women with hypogonadism due to hypopituitarism [16]. Nevertheless, no clear correlation between women's sexual desire and any androgen levels has been established, and the results from cross-sectional settings are inconclusive, showing correlations between different androgens and different aspects of women's sexuality, but none of them consistently [17].

Based on these inconclusive results, questions have arisen regarding whether analysis of androgens is sufficient and whether the questionnaires that were used were adequate [18,19]. As a result, validated questionnaires have been developed, and mass spectrometry (MS) is recommended for steroid analysis in clinical trials [20]. Also debated is if measuring other parameters is necessary to obtain a realistic picture of androgenic activity. In relation to this, Labrie et al. introduced intracrinology, which highlights that a substantial amount of testosterone is metabolized from the inactive precursor dehydroepiandrosterone sulfate (DHEAS) intracellularly in the target tissue and is not present in the peripheral blood, making the total level of bioactive testosterone in the blood difficult to measure. It has therefore been suggested that to obtain a more accurate measure of bioactive androgens, a measurement of androsterone glucuronide (ADT-G) is necessary. ADT-G represents 93% of the degradation products of intracellular androgen turnover and is thought to be a valid (or more accurate) biomarker of overall androgenic activity in female tissues [21]. A study of 121 women with HSDD included the analysis of ADT-G and correlated it with sexual desire. Although ADT-G levels did not differ between women with or without HSDD, the values showed a large variability, and the authors concluded that a larger sample size would be needed for sufficient power to identify differences [19]. Another smaller study investigated the correlation between total androgenic activity and sexual dysfunction in 29 women with breast cancer and found no correlation between sexual function and ADT-G or any other androgens [22].

The activity of the enzyme 17b-hydroxysteroid dehydrogenase, which is important for the transformation of the other inactive precursor androstenedione to testosterone, could also play a significant role in androgen effects in women [19]. This possibility has, to our knowledge, never been investigated and correlated with women's sexual function.

Thus, the research question for the current study was whether or not levels of circulating androgens, including ADT-G, and the activity of 17b-hydroxysteroid dehydrogenase correlate with sexual desire overall in women, or at different life stages. We predicted that the level of ADT-G would show a more consistent correlation than total and free testosterone with sexual desire, given that it is a more accurate biomarker of the total androgenic activity in women as opposed to the level of circulating androgens.

Aims

The primary aim of this study was to evaluate a possible correlation between androgens and sexual desire in healthy women after either age adjustment or stratification into three age groups depending on the intake of systemic hormonal contraception (HC) and postmenopausal HT. The androgens were measured as circulating testosterone, calcu-