THE JOURNAL OF
SEXUAL MEDICINE
INTERNATIONAL CONSULTATION ON SEXUAL MEDICINE REPORTS

Hormones and Female Sexual Dysfunction: Beyond Estrogens and Androgens—Findings From the Fourth International Consultation on Sexual Medicine

Roisin Worsley, MBBS, FRACP,[1] Nanette Santoro, MD,[2] Karen K. Miller, MD,[3] Sharon J. Parish, MD,[4] and Susan R. Davis, MBBS, FRACP, PhD[1]

ABSTRACT

Introduction: In recent years, multiple hormones have been investigated in relation to female sexual function. Because consumers can easily purchase products claiming to contain these hormones, a clear statement regarding the current state of knowledge is required.

Aim: To review the contribution of hormones, other than estrogens and androgens, to female sexual functioning and the evidence that specific endocrinopathies in women are associated with female sexual dysfunction (FSD) and to update the previously published International Society of Sexual Medicine Consensus on this topic.

Methods: The literature was searched using several online databases with an emphasis on studies examining the physiologic role of oxytocin, prolactin, and progesterone in female sexual function and any potential therapeutic effect of these hormones. The association between common endocrine disorders, such as polycystic ovary syndrome, pituitary disorders, and obesity, and FSD also was examined.

Main Outcome Measures: Quality of data published in the literature and recommendations were based on the Grading of Recommendations Assessment, Development and Education system.

Results: There is no evidence to support the use of oxytocin or progesterone for FSD. Treating hyperprolactinemia might lessen FSD. Polycystic ovary syndrome, obesity, and metabolic syndrome could be associated with FSD, but data are limited. There is a strong association between diabetes mellitus and FSD.

Conclusion: Further research is required; in particular, high-quality, large-scale studies of women with common endocrinopathies are needed to determine the impact of these prevalent disorders on female sexual function.

Key Words: Oxytocin; Progesterone; Endocrine Disorder

INTRODUCTION

The endocrine aspects of female sexual function are complex and yet to be fully elucidated. Most research has focused on the role of estrogens and androgens, which have been reviewed in detail elsewhere. As part of the Fourth International Consultation on Sexual Medicine, we judged it was necessary to go beyond the role of estrogens and androgens. This review explores the evidence regarding other hormones that might be implicated in female sexual function. The need for such a review is threefold. First, in recent years research has expanded from a focus on estrogens and androgens to other potential mediators. Second, perhaps partly because of suggestive evidence, women are being prescribed off-label and compounded hormones such as progesterone and oxytocin (OXT).[1,2] Third, given the role of hormones in female sexual function, there is a need to review the effect of common endocrinopathies on sexual function.

METHODS

This narrative review is based on a comprehensive literature search of MEDLINE, SCOPUS, and the Cochrane Library from

Received September 2, 2015. Accepted December 18, 2015.

[1]The Women's Health Research Program, School of Public Health and Preventive Medicine, Melbourne, Victoria, Australia;

[2]Department of Obstetrics and Gynecology, University of Colorado School of Medicine, Aurora, CO, USA;

[3]Neuroendocrine Research Program in Women's Health, Massachusetts General Hospital; Massachusetts General Hospital Neuroendocrine and Pituitary Clinical Center; Harvard Medical School, Boston, MA, USA;

[4]Departments of Clinical Psychiatry Clinical Medicine, Weill Cornell Medical College, New York, NY, USA

http://dx.doi.org/10.1016/j.jsxm.2015.12.014

RECOMMENDATIONS

Based on our review of the literature, we make the following recommendations:

1. The available data are insufficient to support the use of oxytocin for the treatment of female sexual dysfunction (FSD; Grade D).
2. Progestogen-only therapy cannot be recommended for the treatment of FSD (Grade D).
3. Hyperprolactinemia might be a treatable cause of FSD, but data are limited. Prolactin should be measured in any premenopausal woman presenting with sexual dysfunction and amenorrhea and/or galactorrhea (Grade A).
4. Testosterone should not be routinely prescribed to women with hypopituitarism or adrenal insufficiency for the treatment of FSD (Grade B).
5. Dehydroepiandrosterone (DHEA) cannot be recommended for the treatment of sexual interest-arousal disorder in women with adrenal insufficiency or hypopituitarism (Grade B).
6. Polycystic ovary syndrome (PCOS) appears to be associated with decreased sexual satisfaction, but data are limited (Grade D). The effects of treatment of PCOS on sexual function need further research.
7. The paucity of data makes it difficult to draw any conclusions about the association between female sexual function and obesity. In women with FSD and obesity, weight loss appears to be helpful.
8. Metabolic syndrome (MS) might be associated with FSD, but further interventional studies are needed (Grade D).
9. Diabetes types 1 and 2 substantially increase the risk of FSD (Grade A).
10. There is evidence that intensive lifestyle intervention resulting in substantial weight loss can improve sexual function in women with type 2 diabetes. Phosphodiesterase type 5 inhibitors might improve sexual function in women with comorbid type 1 diabetes and arousal disorders (Grade B).

February 2014 through July 2015. We selected publications written in English, mostly from the past 20 years. We also searched the reference lists of articles identified by this search strategy.

Key search terms included *female sexual function, female sexual dysfunction (FSD), oxytocin, progesterone, prolactin, hyperprolactinemia, polycystic ovary syndrome (PCOS), metabolic syndrome (MS), diabetes mellitus, insulin resistance, obesity, thyroid hormone,* and *adrenal insufficiency.* We approached each topic in two ways. We examined whether there was any evidence that the hormone or disease plays a role in FSD, and then we determined whether a clinical recommendation could be made regarding the use of this hormone or the treatment of the disease.

The quality of retrieved data was classified using the Grading of Recommendations Assessment, Development and Education (GRADES) system.

RESULTS

Role of Hormones Other Than Estrogens and Androgens in FSD

Roles of Oxytocin in Female Sexual Function and Dysfunction (Level 5 Evidence)

OXT is a small peptide synthesized in the paraventricular and supraoptic nucleus of the hypothalamus. It is released into the circulation by nerve terminals in the posterior pituitary. OXT facilitates uterine contractions after birth and the breastfeeding "let-down" response. OXT has been implicated as having an important role in affiliative behavior, sexual responsiveness, arousal, and orgasm. The role of OXT in female sexual function is not fully elucidated and appears to be complex. Estradiol increases the expression of OXT and its receptor in the ventromedial hypothalamus of the rat.[3] In rat studies, OXT administration has been found to increase lordosis (sexual receptivity in female rats), with the effect appearing dependent on sex steroids.[4] However, OXT knockouts display normal mating behavior.[4] A group of OXT receptor positive cells has been identified in the medial prefrontal cortex of female mice. Loss of male sexual receptivity in mice has been demonstrated by silencing of these OXT receptors, OXT gene deletion, or infusion of an OXT antagonist.[5]

In small studies of healthy women, serum OXT levels increase significantly after orgasm,[6,7] in keeping with the finding that female orgasm increases blood supply to the pituitary.[8]

In a study of 30 healthy premenopausal women, serum OXT levels were lower in the luteal compared with the follicular phase, with lower levels correlating with lower scores on the lubrication scale of the Female Sexual Function Index (FSFI).[9] In comparison, in the same study, no such fluctuation in OXT levels was seen in the 10 women taking the oral contraceptive pill, although OXT levels correlated with lubrication and arousal.

In a double-blinded placebo-controlled crossover study of 29 healthy heterosexual couples (15 using oral contraceptives), the use of intranasal OXT given 35 minutes before sexual activity resulted in no changes to sexual function in women as measured by the Arizona Sexual Experience Scale but did result in improved ability to share sexual desires and empathize with her partner and decrease tension after intercourse according to the Acute Sexual Experiences Scale.[10] We are not aware of any studies of intranasal OXT in women with sexual dysfunction. The main interest in OXT in humans is its effects on social behaviors, with ongoing research addressing observed sexually differentiated effects on social behavior and emotional responses.[11,12]