Management of Sexual Health in Women with LAM

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- Sexual health in women is frequently unaddressed, and can have a negative impact on the quality of life. Female sexual dysfunction affects approximately 12% of women, with a peak incidence between the ages of 45 and 65 years old.
- The following websites have excellent information for both patients and clinicians: www.menopause.org and www.middlesexmd.com
- The following websites can help in finding local clinicians interested in female sexual health: www.assect.org and www.isswsh.org

Sexual Health for Premenopausal and Perimenopausal Women:

- Perimenopause is a reproductive stage that begins on average between 4 and 6 years before menopause (typically in the mid 40's) and lasts until menopause. Perimenopause is associated with declining ovarian function. Fertility declines, hormone production becomes erratic, and the length and bleeding pattern of menstrual cycles become variable. Serum hormone levels are not helpful to diagnose or confirm perimenopause.
- Sexual health concerns are common during perimenopause; the most common complaint during this time is low desire, also known as hypoactive sexual desire disorder (HSDD).
- Selective serotonin reuptake inhibitors (SSRIs) and serotonin-norepinephrine reuptake inhibitors (SNRIs) are commonly used antidepressants during perimenopause. While highly effective for mood disturbances, these medications can negatively impact sexual health.
- Contraception remains important during perimenopause. Although fertility declines, unplanned pregnancy is not uncommon in this stage of life. LAM patients should be counseled about the risk of unplanned pregnancy during perimenopause and advised to continue to maintain contraception until definite menopause has been achieved. Refer to the contraception guide for various options and their suitability in patients with LAM.

Evaluation and Management:

1. Obtain history regarding menstrual cycles at each visit and determine patient's menstrual status (pre, peri, or postmenopausal).
2. Incorporate one sexual health question, such as: "Do you have any sexual health concerns you would like to address?" into your review of systems while evaluating LAM patients.
3. If the woman reports sexual health concerns, ask about her relationship; if she reports relationship/intimacy issues, referral to a sexual health counselor is appropriate.
4. If the women denies relationship issues, and reports concerns with desire (libido) or orgasmic function evaluate medications that may be contributing, such as antidepressants.
5. All SSRI/SNRI antidepressants impact desire and orgasmic function in varying degrees (Figure 1). Changing SSRI/SNRI, lowering the dose, or adding Bupropion may be beneficial.

Drug	Sexual Desire	Sexual Arousal	Orgasm
Fluoxetine	+++	++	+++
Citalopram	+++	+++	+++
Paroxetine	+++	+++	+++
Sertraline	+++	+++	+++
Venlafaxine	+++	+++	+++
Buproprion	+	+	+
Nefazadone	+	+	+
Vilazodone	+	+	+

Figure 1: Relative impact of various antidepressants on sexual health

6. Flibanserin (Addyi) is currently the only FDA approved medication for HSDD. Flibanserin is a daily oral non-hormonal medication approved for premenopausal women with HSDD. Flibanserin modulates neurotransmitters in the brain that impact desire, similar to antidepressants. Prescribers must be certified, and the medication is contraindicated with alcohol. Although not studied in LAM patients, history of breast cancer is not a contraindication.
7. Testosterone therapy for low desire is supported by data in late perimenopausal women, but there are no FDA-approved testosterone products available. Trial of low dose transdermal testosterone in carefully selected patients may be ok; however, testosterone is aromatized to estradiol in-vivo, and thus careful monitoring of lung function is needed in LAM patients if using transdermal testosterone.
8. Bremelanotide, a novel non-hormonal agent that impacts melanocortin in the CNS, will likely be approved in early 2019 for premenopausal women with HSDD. In contrast to flibanserin, bremelanotide is an on demand medication. Although this agent has not been studied in LAM patients, there will likely be no contraindication for use in breast cancer survivors.

Sexual Health for Postmenopausal Women:

- Menopause marks the end of fertility and is defined by absence of menstrual bleeding for 12 months.
- Genitourinary Syndrome of Menopause (GSM), formerly vulvovaginal atrophy, is the constellation of symptoms, including vaginal dryness, dyspareunia, and recurrent UTI's, most women experience after menopause. These symptoms are related to changes in vulvovaginal tissue related to the loss of estrogen with menopause, and worsen over time.

<u>Evaluation and Management</u>

1. Non-hormonal moisturizers and lubricants are first line therapy for all women with GSM. Local vaginal estrogen is the gold standard for treatment of GSM. Vaginal estrogen creams do not raise serum estrogen levels above the postmenopausal level (<20pg/ml), and are safe to use in patients with LAM (Figures 2 and 3).
2. The lowest available FDA approved vaginal estrogen therapy (Imvexxy 4mcg gel caps) delivers 0.5mg estradiol over the course of a year. This equates to the estradiol in one half of one single birth control pill. Max serum estradiol levels with Imvexxy 4mcg (package insert) is 4.8 pg/dl well below the postmenopausal level of <20pg/ml.
3. Vaginal Prasterone (DHEA, brand name Intrarosa), approved in 2017, is a non-estrogen steroid that is converted to estrogen and testosterone. Maximum serum estradiol levels with Intrarosa (package insert) is 5.04pg/ml, similar to Imvexxy.
4. Vaginal CO2 laser is a widely available energy based treatment (not covered by insurance in the US, average cost $2000 for series of 3 treatments) with small clinical trials supporting efficacy and safety.

Activity	Regular sexual activity Solo, partner, device Dilators Pelvic floor physical therapy
Non Hormonal	Lubricants Moisturizers Topical Lidocaine Laser
Hormonal	Vaginal estrogen therapy Vaginal DHEA Ospemifene Systemic estrogen therapy

Figure 2: Treatment options for GSM

Type		Product name	Starting Dose	Maintenance Dose	ANNUAL DOSE ESTRADIOL	Serum Estradiol Level (Post Menopause <20 pg/ml)
Vaginal Cream	**17B-estradiol**	**Estrace, Generic**	0.5-1gm/d x 2 week	0.5-1 gm 1-3x week	***Approx 7 mg per year***	
	Conjugated estrogens	Premarin	0.5-1gm/d x 2 week	0.5-1 gm 1-3x week		
Vaginal Inserts	**17B estradiol gel caps**	**Imvexxy**	4 or 10 mcg/d for 2 weeks	4 or 10 mcg/d 2 x week	***0.5 mg /year (4mcg gel caps)***	***4.8 pg/ml (4 mcg gel caps)***
	Estradiol Hemihydrate	**Vagifem, Yuvafem**	10 mcg/d for 2 weeks	10 mcg/d 2 x week	***Approx 1 mg per year***	**8.0pg/ml (using 10mcg Vagifem)**
	DHEA	**Intrarosa**	6.5mg/d	6.5 mg day		
Vaginal Ring	**17B-estradiol**	**Estring**	2 mg releases 7.5mcg/d	Change every 90 days	***Approx 2.7 mg per year***	***4.6pg/ml***
OCP's	**Estradiol**			**1mg/d**	***365 mg/year***	

Figure 3: Comparison of commonly used local vaginal estrogen options

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