SEXUALITY AND CANCER SURVIVORSHIP IN WOMEN

Annual Scientific Meeting of SMSNA
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Disclosures

- Advisory Boards
  - Emotional Brain, Pfizer, Palatin, SST Pharmaceuticals

- Speaker
  - Pfizer
Objectives

- Describe the key physiologic, psychologic, and social effects of treatment on sexual health of cancer survivors

- Discuss strategies clinicians can use to address sexual health concerns of cancer survivors, with a focus on breast cancer
Case: Premenopausal Breast Cancer Patient

- 34 year female, 3.5 cm mass, lymph node positive: underwent chemotherapy, radiation, bilateral mastectomy

- Pre-diagnosis: seeing me with partner for treatment of premature ejaculation with couple issues

- What will be the impact of breast cancer on her sexual function?
Female Sexual Disorders: DSM-5, ICSM, ISSWSH Nomenclature

A clinically significant disturbance in a person’s ability to respond sexually or to experience sexual pleasure

**DSM-5**
- Sexual Interest/Arousal Disorder
- Orgasm Disorder
- Genito-Pelvic Pain/Penetration Disorder

**ICSM, ISSWSH**
- Hypoactive Sexual Desire Disorder
- Genital Arousal Disorder
- Persistent Genital Arousal Disorder
- Orgasm Disorders (Premature, PDOD, POIS)
- Sexual Pain-Penetration Disorder

40-100% cancer survivors experience sexual dysfunction, 50% breast cancer patients, extent and type vary based on diagnosis and treatment
Cancer Treatment and Sexual Dysfunction

**SURGERY**
- Resection of sexual structures
- Damage to surrounding tissues

**RADIATION**
- Fibrosis
  - Impact dependent on organ, volume, dose

**CHEMOTHERAPY**
- Gonadotoxicity
  - Impact dependent on drug and dose

**ENDOCRINE THERAPY**
- Alterations in hormonal environment

**Resection/damage/dysfunction of gonads**
Cancer Treatment and Sexual Dysfunction

Resection/damage/dysfunction of ovaries

Loss of estrogen

Premature Ovarian Failure

Infertility

Menopause

Menopausal Symptoms

- **Systemic**: hot flashes, sleep disturbance, mood changes
- **Vaginal**: narrowing, shortening, loss of elasticity, atrophy, dryness, pain
Premenopausal women: transient or permanent amenorrhea resulting in menopausal symptoms such as:

- Hot flashes
- Vaginal dryness
- Dyspareunia
- Decreased libido
- Changes in sexual response
Sexual Side Effects

▪ Postmenopausal women:
  ▪ AIs suppress estrogen to sub-physiologic levels
  ▪ Symptoms similar to premenopausal women

▪ Estrogen depletion leads to instability of the hypothalamic thermoregulatory set-point
  ▪ Allows changes in body temperatures
  ▪ Hot flushing sensations

▪ Hot flashes and sexual dysfunction profoundly affect QOL and may affect compliance with treatment.
Psychologic and Social Issues

- Physiologic changes can alter body image
  - Feeling unattractive or damaged can affect self-esteem and perception of self as sexual being
- Depression $\rightarrow$ ↓ desire/pleasure
- Prior relationship will affect couple’s adjustment
- Social challenges
  - Anxiety about exposing self with altered appearance or performance
  - Partner concerns about pain or fatigue
  - “Intimacy overload”
  - Patients without partners may be reluctant to form new relationships
<table>
<thead>
<tr>
<th>Most Common Sexual Problems</th>
<th>Prevalence</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>30%–100%</td>
<td>Sadovsky et al.</td>
</tr>
<tr>
<td>Overall</td>
<td>76%</td>
<td>Goldfarb et al.</td>
</tr>
<tr>
<td>Desire</td>
<td>23%–64%</td>
<td>Bloom et al., Arora et al., Fobair and Spiegel, Barni and Mondin, Burwell et al.</td>
</tr>
<tr>
<td>Arousal or lubrication</td>
<td>20%–48%</td>
<td></td>
</tr>
<tr>
<td>Orgasm</td>
<td>16%–36%</td>
<td>Fobair et al., Figueiredo et al.</td>
</tr>
<tr>
<td>Pain/dyspareunia</td>
<td>35%–38%</td>
<td></td>
</tr>
<tr>
<td>Body image concerns</td>
<td>30%–67%</td>
<td></td>
</tr>
<tr>
<td>Poor nipple sensation</td>
<td>&gt; 90%</td>
<td>Djohan et al.</td>
</tr>
</tbody>
</table>

Bober and Varela, JCO, 2012
## Endocrine Therapy and Sexuality

<table>
<thead>
<tr>
<th></th>
<th>Tamoxifen</th>
<th>Aromatase Inhibitors</th>
<th>Fulvestrant</th>
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</thead>
<tbody>
<tr>
<td>Vaginal Dryness</td>
<td>+</td>
<td>++</td>
<td>+</td>
</tr>
<tr>
<td>Vaginal Discharge</td>
<td>+</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vaginal/Endometrial Bleeding</td>
<td>+</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vaginitis</td>
<td>+</td>
<td>++</td>
<td>+</td>
</tr>
<tr>
<td>Dyspareunia</td>
<td>+</td>
<td>++</td>
<td>+</td>
</tr>
<tr>
<td>Vulvar changes</td>
<td></td>
<td>++</td>
<td></td>
</tr>
<tr>
<td>Urogenital atrophy</td>
<td></td>
<td>++</td>
<td></td>
</tr>
<tr>
<td>Hot flashes</td>
<td>++</td>
<td>++</td>
<td>+</td>
</tr>
<tr>
<td>Decreased libido</td>
<td>++</td>
<td>++</td>
<td>++</td>
</tr>
</tbody>
</table>
Strategies To Address Sexual Health Concerns of Cancer Survivors
NCCN Guidelines For Survivorship

- Conduct more thorough assessment of patients who have concerns
  - Specific dysfunction (desire, arousal, orgasmic, pain)
  - Prior cancer treatment that is associated with menopause or affect sexual function
  - Psychosocial problems – depression, anxiety, relationship issues
  - Traditional risk factors – comorbidities, medications, lifestyle behaviors
  - GYN examination – tenderness, atrophy

NCCN, 2013
Treatment Options For Hot Flashes

- **Non-hormonal**
  - Anti-depressants: SSRIs and SNRIs
    * paroxetine mesylate (7.5 mg), fluoxetine, sertraline, venlafaxine; * No sexual side effects
  - Neurologic agents: gabapentin, pregabalin
  - Centrally acting adrenergic agonists: clonidine, methyldopa

- Supplements: isoflavone extracts & herbs (RCTs are negative); vitamin E 400-800IU daily

- Non-pharmacologic: relaxation, acupuncture

- Hormonal: estrogen, progestin

FSD: Available Treatments

- **Water-based lubricants**
  - Improve dryness, decreases pain with intercourse and minimizes friction & irritation
  - Short duration of action/need to be applied frequently
  - Safe to use with condoms
  - Used as needed
  - KY Jelly, Astroglide, Liquid silk, Eros for Women

- **Silicone-based lubricants**
  - **Longer lasting than water-based lubricants**
  - Safe to use with condoms
  - Can’t use with silicone toys
  - Used as needed
  - KY Intrigue, Eros Body Glide, Wet Platinum Silver

Derzko, Current Oncology, 2007; Goldfarb, Seminars in Oncology, 2013
FSD: Available Treatments

- **Vaginal moisturizers**
  - Hydrate vaginal tissue
  - **Implements dryness, pruritus, elasticity, and irritation**
  - Replens, Hyaluronic Acid, Vitamin E
  - Used every 2-3 days
  - Takes 2 months to see full benefit

- **Counseling and/or sex therapy**
  - Understand impact of treatment effects on sexuality
  - Increase sexual knowledge/expand sexual repertoire
  - Reduce fear about intimacy
  - Learn strategies to address pain (i.e. dilator therapy)
  - Promote positive sexual identity

Derzko, Current Oncology, 2007; Chlebowski, Clinical Breast Cancer, 2009; Goldfarb et al, Seminars in Oncology, 2013
<table>
<thead>
<tr>
<th>Product</th>
<th>Ingredients</th>
<th>Use</th>
<th>Price</th>
<th>Studies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Replens</td>
<td>Polycarbophil (Glycerin, mineral oil)</td>
<td>Every 3 days</td>
<td>$17.5/14 app</td>
<td>Yes</td>
</tr>
<tr>
<td>LUVENTA</td>
<td>Lactoperoxidase Lactoferrin</td>
<td>2x/wk</td>
<td>$20/ 5 app</td>
<td>Yes</td>
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<tr>
<td>KY Liquibeads (ovules)</td>
<td>Dimethicone, Gelatin, Glycerin, Dimethiconol</td>
<td>1-7d/wk</td>
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<td>No</td>
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<tr>
<td>KY long lasting</td>
<td>Various polymers (Glycerin, mineral oil)</td>
<td>2-3x/wk</td>
<td>$16/6 app</td>
<td>No</td>
</tr>
<tr>
<td>Emerita personal</td>
<td>Aloe Vera Gel, Calendula, Vitamin E, Ginseng, Chamomile,</td>
<td>As needed</td>
<td>$16/4 oz</td>
<td>No</td>
</tr>
<tr>
<td>moisturizer</td>
<td>Allantoin</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Moist again</td>
<td>Carbomer, aloe (glycerin, chlorhexidine)</td>
<td>As needed</td>
<td>$7/4 oz</td>
<td>No</td>
</tr>
<tr>
<td>Hyalofemme</td>
<td>Hyaluronic acid</td>
<td>7 days &gt; 2/wk</td>
<td>$17/30gram</td>
<td>HA-yes</td>
</tr>
<tr>
<td>Hyalogyn</td>
<td>Hyaluronic acid</td>
<td>2-3x/wk</td>
<td>$25/30 days</td>
<td>Yes</td>
</tr>
</tbody>
</table>
FSD: Available Treatments

- Pelvic Floor therapy
  - Stretches and relaxes pelvic floor muscles
  - Improves control and strength of pelvic muscles
  - Used to decrease pain with intercourse or gyn exams
  - May promote circulation and pelvic blood flow
  - May include dilator therapy
  - Daily use recommended

- Intravaginal estrogens
  - Re-estrogenizes the vaginal epithelium
  - Most effective therapy for vaginal dryness/atrophy
  - Causes at least a transient estradiol elevation

Kendall et al., Annals of Oncology, 2006; Goldfarb et al, Seminars in Oncology 2013; Chlebowski et al., Clinical Breast Cancer, 2009
# FDA Approved Intravaginal Estrogens For Postmenopausal Women

<table>
<thead>
<tr>
<th>Name</th>
<th>Dose</th>
<th>Typical Serum Level (pg/ml)</th>
<th>Maximum Annual Delivered Systemic Dose (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>17-β Estradiol tablets</td>
<td>10 mcg daily for 2 weeks then twice weekly</td>
<td>4.6</td>
<td>1.14</td>
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<tr>
<td>Estradiol vaginal ring</td>
<td>7.5mcg daily inserted every 90 days</td>
<td>8.0</td>
<td>2.74</td>
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<tr>
<td>Estradiol cream</td>
<td>2-4 g/d for 1-2 weeks then titrated to 1gm 1-3 times weekly</td>
<td>Variable</td>
<td>7.1</td>
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<tr>
<td>Conjugated equine estrogen cream</td>
<td>2-4 g/d for 1-2 weeks then titrated to 1gm 2-3 times weekly</td>
<td>Variable</td>
<td>Variable</td>
</tr>
</tbody>
</table>

Pruthi et. al, The Breast Journal 2011
Serum Estradiol Levels in Women Receiving Concurrent Aromatase Inhibitors and Vagifem

Kendall et al., Ann Oncol, 2006
Al or Tamoxifen with Intravaginal Estrogen Ring

Shannon Wills et al. JOP 2012;8:144-148
Improvement In Sexual Function Domains As Measured By Female Sexual Function Index

* Indicates a statistically significant improvement

Goldfarb, ASCO, 2014
Vaginal Tablet – Safety and Efficacy

- Intravaginal 10µg Vagifem® provided statistically significant improvement in sexual dysfunction specifically in the domains of desire, pain, lubrication, orgasm and satisfaction
- With atrophic vaginal and vulvar mucosa, systemic absorption will initially be high; but after mucosa thickens, systemic absorption is limited (24 weeks total)
- With tablet and ring, systemic dose is comparable to level seen after natural menopause
- Use in women with estrogen-sensitive cancers is controversial

Goldfarb, SABCS abstract P2-12-05, 2013
FDA approved for atrophic vaginitis due to menopause
  ▪ 17-β estradiol tablets

FDA approved for moderate to severe dyspareunia, a symptom of vulvovaginal atrophy
  ▪ Estradiol ring
  ▪ Estradiol cream
  ▪ Conjugated equine cream
  ▪ Ospemifene (SERM) - first non estrogen oral tablet

FDA approved for acquired, generalized HSDD in premenopausal women - first drug for decreased libido
  ▪ Flibanserin

Drugs In Development:
  ▪ Lybridio - Intravaginal testosterone
  ▪ Lybridos - Intravaginal DHEA
  ▪ Bremelanotide - Transdermal testosterone
Conclusions

- Breast and gynecological cancer treatment impact sexual function.
- Sexual dysfunction is prevalent in women with cancer.
- SSRIs and other nonhormonal agents improve hot flashes.
- Supportive measures including lubricants, moisturizers, dilators, physical therapy and counseling may help.
- Safety of vaginal estrogen unclear – await further testing.
- Need rigorous testing of available interventions in randomized controlled trials, ie flibanserin, ospemifene.
- New drugs in development may help cancer survivors’ sexual symptoms.