Drug therapy applied to sexuality

Impact of POP surgery on female sexuality

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Female sexual dysfunction

• Desire disorders
• Arousal disorders
• Orgasmic disorders
• Pain
• Non coital pain disorders
• Causes personal distress
Physiology of sex

Desire → Physical changes
Physiology of sex

Desire

Physical changes

Model of female sexuality

Physiology of sex

Desire → Physical changes

Attitude → Aptitude
Female sexual dysfunction

- Desire disorders
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- Orgasmic disorders
- Pain
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- Causes personal distress

Etiology:
- Organic
- Psychological
- Mixed
- Uncertain
- Primary
- Secondary

Can drugs be the solution?
Physiology of sex

Vasocongestion, engorgement

Sildenafil in postmenopausal women

- Open label, non-randomized trial, 3 months
- Self-described FSD
- Outcomes:
  - New instrument: Index of Female Sexual Function (IFSF)
  - Global efficacy question
- Results:
  - Mean usage: 3.1/week
  - Only 18% had significant improvement in IFSF score (>60%)
  - Physical changes noted, incl. clitoral sensitivity (hyper in 21%)

Kaplan S. Urology 1999;53:481
Sildanefil in premenopausal women with arousal disorder

- Double cross-over
- Viagra 25 mg, 50 mg, placebo
- Outcomes:
  - Personal Experiences Questionnaire (arousal, orgasm, enjoyment, frequency, fantasies)
- 51 women, used pill 2.7x/week
- Results: All parameters improved with Viagra
  - Arousal, orgasm (p<0.001)
  - Fantasies, intercourse, enjoyment (p<0.05)
  - No difference between Viagra doses.

Caruso S, Intelisano G. BJOG 2001;108:623

Sildanefil in women with FSD with arousal disorder

- RCT Viagra vs. matching placebo
- Outcome:
  - Sexual function questionnaire (SFQ)
  - Sexual activity event log
  - Life Satisfaction Checklist (LSC)
  - Global efficacy questions (2)
- 577 estrogenized, 204 estrogen-deficient
  - 50% with primary arousal disorder
- Results: No significant differences in any parameters

Sildanefil in FSAD

- Double blind, placebo-controlled
- Postmenopausal women, on ERT and/or TRT
- Viagra (50 mg, adjustable to 100 or 25)
- Outcomes:
  - Female Intervention Efficacy Index (FIEI), questions: 2 (increased sensation) and 4 (increased satisfaction)
- Results: significant improvements with Viagra
- No improvements in women with HSDD

Berman JR, Berman LA. J Urol 2003;170:2333

Sildanefil in healthy volunteers

- 68 healthy volunteers without FSD
- Double-blind, cross-over – Viagra 50 mg/placebo
- Outcomes:
  - Personal Experiences Questionnaire (PEQ)
- Results:
  - Viagra improved arousal, orgasm, enjoyment, including improvement in baseline.
Viagra: Assessing the mechanism of action

- Non-contrast pelvic MRI to assess clitoral engorgement (normal 50-300%)
- 19 premenopausal women with FSAD, received Viagra 100mg, then placebo placebo
- Results: at 60 mins. >50% engorgement
  - Viagra: 89%
  - Placebo: 84%
- Conclusions:
  - Viagra did not augment genital response
  - FSAD not primary engorgement disorder

Leddy LS, Yang CC. J Sex Med 2012 May 23;epub

Viagra may be useful in some women, but....

- Data is unclear
  - Possible benefit – 8 studies
  - No benefit – 4 studies
- Studies lack uniformity
  - Small sample sizes
  - Used inappropriate statistical tests
  - Non-validated assessment instruments
- There are subgroups where efficacy has been demonstrated

When is Viagra useful?

Proven efficacy in women with:

• **MS**

• **Type 1 DM**
  – Caruso. Fertil Steril 2006;85:1496

• **Spinal cord injury**

• **On antidepressant meds**
  – Numberg. JAMA 2008;300:395

What else is in the drug cabinet?
Management of vaginal atrophy

• Local estrogen – cream/tablets/ring
• Systemic ERT/HRT
  – Preceded by local e2
• Systemic E + SERM – pts. with uterus
  – CE + bazedoxifine (Duavee)
• E agonist/antagonist
  – Ospemifene (Osphena) – indic: dyspareunia
• Non-hormonal therapy

Physiology of sex

Desire

Physical changes
How to improve women’s desire?

Androgens to increase libido

• Testosterone
• Tibolone
• DHEA

• must be estrogen-primed
Testosterone patch RCT

- Randomized, placebo-controlled, double-blind 24 week study, T patch (Intimate SM 1)
- 562 women with HSDD, post BSO, on ERT enrolled
- Outcomes:
  - Frequency of total satisfying sexual activity
  - Sexual function endpoints
- Results:
  - Increase satisfying sexual activity (p=0.0003)
  - Improvement in desire and decrease distress.
  - Safety similar

Simon J. J Clin Endocrinol Metab 2005;90:5226

TD T in women with BSO

- 75 women s/p TAHBSO on po ERT (CE)
- Randomized, placebo-controlled, 12 weeks
- Groups: placebo, 150 or 300 microgm.
- Outcomes:
  - Brief Index of Sexual Function in Women
  - Psychological General Well-being Index
  - Diary (via phone)
- Results:
  - Free T increased from 1.2 pg/ml to 3.9/5.9
  - Significant placebo effect
  - 300 microgm – increased frequency, genral well-being
  - Diary no change

Shifren JL. NEJM 2000;343:682
Testosterone spray

- Randomized, double-blind, placebo controlled
- 261 premenopausal women, T<3.8 pmol/L – reported decrease in satisfying sexual activity
- Outcomes:
  - Self-reported satisfying sexual events (SSE)
  - Sabbatsberg Sexual Self-rating Scale, Psychological Well-Being Index
- Results
  - At various doses, only 90 microL spray was superior to placebo, higher and lower were not
  - Improved 0.8 SSE per month
  - Placebo effect high


Testosterone therapy

- No T-only product FDA approved in US yet
- Concerns re: long term safety
- Testosterone levels not correlated with sexual well-being
- Very strong placebo effect
- Off label use – pellets, compounded, i.m. T, etc. – cautioned
- NAMS position statement 2014 - selective
Physiology of sex

Data is unclear, but....
POP surgery and female sexuality

Overall:

Pts. should expect some dyspareunia after POP surgery – especially if:

- Vaginal anatomy not normal
- Atrophy
- Infrequent sexual activity (pre &/or post)
- HSDD
- Posterior repair
Vaginal stricture formation

- Typically posterior distal
- Firms up over time
- If soft: e2 cream and sex
- If firm: e2 cream and release

Mesh exposure
Sexual dysfunction after kit

• 0%, 15/120 preop resolved
  – 120 Apo/Peri, 1 yr., 93% cure, erosion 3%
  Garauder-Burmester (IUJ 2006)

• 16.7% de novo, 4/8 preop resolved
  – 129 Prolift, 1 yr., erosions 16.3%
  Lowman (AJOG 2008)

• 9% de novo
  – 68 Prolift, 1 yr., 86.6% cure, erosions 2%
  Wetta (IUJ 2009)

• 18% de novo, 28% resolution of preop
  – 46 Prolift, 1 yr., 91% cure, erosions 15%
  Milani (IUJ 2009)

• Worsening PISQ-12 score (15.5 to 11.7)
  – Mainly in behavioral-emotive, partner-related items
  – 84 Prolift (cohort 261), 1 yr.
  Altman (Obstet Gynecol 2009)

Prolift 1 yr. data

• Prospective trial, 46 patients
• Continuous piece PP mesh
  – Anterior and posterior dissections, sub-apex bridge tunneling
• Anatomic success – 91%
  – Apex: st. 0 – 80% st. 1 – 15.6%
  – Anterior: st. 0 – 69% st. 1 – 26.7%
• Marked improvement QOL
  – UDI, IIQ, DDI
• Dyspareunia – no increase pre-post (37%)
  – de novo 18%, resolved 28%
• Erosion rate – 15%
  Milani A, Vierhout M. Int Urogynecol J 2009;20:1203
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Mesh contraction

- 17 pts. operated on for mesh contraction
- Symptoms
  - Pain (100%)
  - Dyspareunia (100%)
  - Discharge/spotting (18%)
- Physical exam
  - Focal tenderness (100%)
  - Tender bands (82%)
  - Tightness (41%)
  - Foreshortened vagina (29%)
  - Erosion (53%)
- Management
  - Mesh mobilization and division of fixation arms
- Results
  - Pain resolution (88%)
  - Dyspareunia resolution (64%)

Feiner B, Maher C. Obstet Gynecol 2010;115:325
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PISQ-IUGA Revision (PISQ-IR)
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Pelvic Organ Prolapse/Urinary Incontinence and Sexual Function (PISQ-12)

• Condition-specific questionnaire to evaluate Sexual function in women with UI and/or POP
  – Use only in women who are sexually active with POP or UI
• 12 questions generated from a 31 item long form (regression analysis)
  – Validated and correlated with several validated questionnaires
    – IIQ-7, SHF-12, Symptom questionnaire Depression scale
• Domains
  – Behavioral/Emotive factor (4)
  – Physical factor (5)
  – Partner-Related factor (3)
• 5 point Lickert scale never to always
• Scores calculated by totaling the score for each question
• The Higher the score the BETTER the sexual function
• Higher scores in patients without POP/UI vs. patients with POP/UI.

Rogers GR et al Int Urogynecol J 2003 12:164-168
Sexual Function After Surgery for SUI and/or POP: A multi-center prospective trial

- 102/269 women completed questionnaire
  - Underwent Prolapse/Incontinence surgery
- Pre-op PE, POPQ, UDS, PISQ & IIQ7
- Follow up 3, 6 months post-op
- 75/102 (74%) completed questionnaire pre- & post-op
- Results: Decline in PISQ scores after POP/UI surgery
  - 22/75 (22%) reported improved PISQ scores
  - 53/75 (71%) reported worsening of symptoms- lower PISQ scores
- Greatest decline in Behavioral (sexual desire), greatest improvement in Physical (fear of loss of urine during sex)


**PISQ-IR**

- IUGA revision of PISQ-12
- Emphasis on:
  - Impact on patient
  - Impact on non-”sexually active” (40+%)  
- Validation (US/UK) completed
- International validation under way
- Non-English validation
  - Spanish, Japanese, Portuguese, Turkish, French

