Menopause Update:
Hot Off the Press
Focus on
Hot Flashes, Atrophic Vaginitis

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Onset, Massachusetts
Mimi Secor, DNP, FNP-BC, FAANP

- FNP for 41 years specializing in Women’s Health
- National Speaker, Educator, Entrepreneur, Health Advocate
- 2013 Lifetime Achievement Award, (Mass Coalition of NPs)

- DNP-2015, Rocky Mountain University, Provo, Utah

- Nov 2016 First Bodybuilding competition, 5th place
- July 28, 2018, Fourth Competition, 2nd in over 55
- New book, “Debut a New You: Transforming Your Life at Any Age”, #1 International Best Seller

- Working w/ my daughter as “Coach Kat and Dr Mimi”
  Helping NPs/PAs become Healthy and Fit

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Menopause Update: Focus on Hot Flashes, Atrophic Vaginitis

• I will **NOT** discuss off label use or investigational use in my presentation:

• I **HAVE** financial relationships to disclose:

  Honoraria from: Duchesney, Osphena for VVA
Menopause Update: Objectives

• Describe epidemiology of menopause, Vasomotor Symptoms (VMS) and Vulvovaginal Atrophy (VVA) 15 mins
• Discuss diagnosis of VMS and Vulvovaginal Atrophy 15 mins
• Explain options for treatment of VMS and VVA 30 mins
Menopause Diagnosis
52 Million in 2010: 6,000 day

• Average age 50-52 years
• 12 months since FMP (final menstrual period)
• NO labs needed
• FSH over 30 mIU/m
  • 1 week off CHC*, or 1 month if inconclusive
• Estradiol < 20 pg/ml
• Vasomotor symptoms
• Contraception x 12 months after FMP!!!

*CHC/ combination contraceptive contraceptive

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Vasomotor Symptoms (VMS) 
Epidemiology: COMMON

- 75% of perimenopausal women experience these
- Caused by fluctuations in hormones
- BUT exact mechanism unclear

- Duration x 6 months- 2 years, up to 5-12+ years !!!
- Average duration 4-7 years
- 10-25% C/o severe symptoms,
- If severe sx in perimenopause- duration 11+ years
- May be a marker for subclinical CVD!
- Ethnic variation: African American 46%, Japanese 18%
- Surgical menopause = More severe symptoms!!!
Early Menopause Complications:

• If untreated:
  • Higher rate of dementia
  • Neurocognitive decline
  • Parkinson’s

• VMS assoc. w/ massive blood flow shift in the brain!
  • NOT GOOD FOR Brain Function- or Cognition

• Exacerbated by sleep disturbances!!!
Vasomotor Symptoms: Worsened by...

• Undiagnosed or Inadequately Treated:
  • Diabetes
  • Thyroid disease
Hot Flashes/VMS and CVD

• Frequent, severe and bothersome;
• May be marker for Subclinical CVD

• 2 fold increased risk of developing CVD over 14 years

Swan Study
VMS: Non-Pharmacologic

• Dress in layers
• Cool bedroom, chilling pillows, sheets
• **Healthy body weight**
• Avoid smoking
  • Incr. estrogen metabolism = incr. VMS
• **Avoid triggers**: (personal)
  • hot drinks, caffeine, spicy foods, ETOH, emotional reactions!
VMS: Non-Pharmacologic Self-Care: Variable Efficacy

• Paced respirations - effective
• Exercise
• Yoga
• Acupuncture

• Massage
• Other self-care options

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• Isoflavones (Soy): modestly effective
• Black Cohosh: NOT effective (Remifemin): Studies pending
• Progesterone cream: OTC, unclear efficacy, safety, esp. endometrial effects (poorly absorbed transdermally)
Estrogen for VMS per NAMS

- Benefits of HT/ET*
- more likely to outweigh risks for symptomatic women < 60 years (occult CVD)
  or within 10 years since FMP

*(Hormone Therapy, Estrogen Therapy)
NAMS, 2017
HT* for VMS: Risk per NAMS

• Incr. Risk of VTE & Ischemic Stroke w/ Oral HT but absolute risk is very LOW < 60 years

• Dose, duration
  • consistent with treatment goals &
  • safety issues &
  • should be individualized

• “Shortest period of time and lowest dose”

*Hormone therapy = Estrogen, Progesterone/progestin

NAMS, 2017
HT for VMS: Risk Breast Cancer

- Risk >50 years associated with HT is a complex issue!!!

- Increased risk is primarily associated w/ addition of progestogen (MPA) to estrogen and duration of use

- Risk is small and decreases after treatment is stopped
- No increase w/ Estrogen-only (CEE) up to 7.1 years

- Increase w/ (estrogen/progestin) group after 3-5 years
VMS Treatment Options

Hormonal
- Estrogen

Non-Hormonal
- Non-estrogen
VMS: Treatments
Systemic Estrogen for VMS

• Systemic estrogen; Oral, Vaginal, Transdermal
• Estrogen (versus non-estrogen)
• Very effective
• Safer in early post-menopause (within 10 y)
• Less safe age 70 and over
• Less safe as BMI increases
• “Lowest dose for the shortest duration”

NAMS, www.menopause.org

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VMS: Treatments- Estrogen Systemic for VMS

• Oral:
  Estrogen (Premarin, Estrace) 0.625-0.4, 0.3 mg
  Progesterone (Prometrium) 100-200 mg @hs

• Transdermal: SAFER per Observational studies
  Steady blood levels, lower dose, possibly wt gain & libido neutral !!!
  Estradiol Patch (Vivelle, Climara, etc.)
  Estradiol Gel (Estragel, DiviGel (3 doses), etc.)
  Estradiol Spray (Evamist) 1-3 sprays to forearm in AM (biphasic pharmacokinetic curve = 2 doses)

• Ring: Estradiol (FemRing) every 3 months
NAMS: Bioidentical Hormones- What’s the Truth?

• Compounded vs FDA Approved:
  
  Compounded: Lack of research!

  • Safety, Efficacy, Dosing: UNCLEAR

  FDA approved: Robust literature
  Estradiol (Estrace)
  Progesterone (Prometrium)
Bioidentical Hormones: FDA Approved Options

Pharmaceutical, FDA approved:
• Estradiol: Oral, transdermal, vaginal
• Progesterone: Oral

Non-Pharmaceutical, NOT FDA approved: CAUTION!!!
• Compounded estrogen, progesterone, testosterone
• Progesterone cream: Over-the-counter

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Newer Medications: FDA Approved

• **Paroxotine (Brisdelle)**: (7.5 mg): 1st non-hormonal Rx (SSRI) for moderate to severe VMS (hot flashes) (Paxil)

• **Conjugated Equine Estrogen/Bazedoxifene (DuaVee)**: Combination estrogen/SERM for moderate to severe VMS

• **Ospemifene (Osphena)**: Non-estrogen (SERM) to treat moderate to severe dyspareunia due to VVA in menopause

• **DHEA (Intrarosa)**: 6.5% PV suppositories qd

• **Estrogen (NEW Imvexxy)**: PV inserts x2 wk
Paroxitene* (Brisdelle) Low Dose

• FDA approved for VMS/ hot flashes
• Dosing 7.5 mg PO daily
• Effective, safe, few side effects
• Alternative: if estrogen contraindicated
• Possible reduced anxiety
• Avoid with Tamoxifen
  Potential for interaction w/ cytochrome P-450 2D6 inhibitors

*Paxil (brand name)
Non-Hormonal Options for Managing Vasomotor Flushes: SSRIs, SNRIs: Off-label

- **Venlafexine (Effexor XR):** 37.5 mg a day-titrated as needed; Average dose 75 mg/day
- **Desvenlafexine (Pristiq):** 50-100 mg/day
  - Studied extensively
  - 4 randomized, placebo controlled trials found significant reduction of VMS at 100 mg daily!

  (Speroff et al., 2008; Archer et al., 2009; Archer et al., 2009; Pickar et al., 2007).
Non-Hormonal Options for VMS: Off-label

• **Clonidine (Transdermal):** centrally acting, for Rx of HTN.
  • Studied more extensively in 1970s-1990s
  • Reporting mixed results in reducing VMS
  • Trial using clonidine for patients on tamoxifen therapy showed a 38% reduction in hot flushes per day (Pandya et al., 2000)

• **Clonidine (Oral):**
  • Initial oral dose for hot flash treatment is 0.05 mg twice daily, but some women may require at least 0.1 mg twice daily
  • Modest effect on symptoms, adverse side effects (insomnia, dry mouth, constipation, drowsiness.)

• **Hypertension also:** May be a good choice
Non-Hormonal Options for VMS: Off-label

- **Gabapentin** indicated in treatment of partial seizures and post herpetic neuralgia; studied in Hot Flash reduction

  - Initiated at a daily dose of 300 mg at HS
  - Can be increased to 300 mg twice daily and then to 3 times daily at 3- to 4-day intervals.
  - Pandya et al., (2005) studied with breast cancer patients (n=420) **hot flush frequency was reduced by 44%** at 900mg/day.
  - Studied: titrated to an 1800 mg daily dose, taken orally, 600 mg with the morning meal and 1200 mg with the evening meal.
  - Adverse effects: **dizziness**, somnolence, peripheral edema, **weight gain**

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VMS: Patient Education

• Must be thorough, empathetic, resourceful
• Handouts, websites, etc.

• Menopause.org (NAMS)
• NAMS certification

As a NCMP

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Vulvovaginal Atrophy (VVA) = Atrophic Vaginitis (AV) = “Genitourinary Syndrome of Menopause (GSM)”

1/3 of menopausal women affected

• Irritation
• Dryness
• **Dyspareunia** !!! (superficial vs deep?)
• Discharge- variable

• **Urinary symptoms**: Dysuria, urgency, frequency, UTIs, incontinence
Vulvitis: Need to Clarify!!!
Vaginal, Cutaneous Yeast, Contact, Allergic, Other
VVA/GSM

• Vulva
  ‘Sticky glove sign’
• Erythema, mottling
• Pallor
• Flattening of rugae
• Leukorrhea variable!!!
  Esp. amount
• Mimics BV, Trich, HSV
other etiologies
Diagnostic Work up of VVA, GSM

- **Vaginal pH elevated** > 4.8
  - Proxy test for estrogen levels = maturation index
- **Negative Amine KOH ”Whiff “test**
- Few Lactobacilli
- Mixed bacteria, grainy epithelial cells
- WBCs variable
- **Immature epithelial cells**, maturation index
- Avoid non-specific vaginal cultures, Pap inaccurate
- STI testing as appropriate!
NEW: Vaginal pH Swab Test (VS-Sense)

negative    positive
Figure 19-11. Different histologic layers of vaginal stratified squamous epithelium. (From Naib Z. Exfoliative Cytology. Cytology. 3rd ed. Boston, Mass: Little, Brown; 1985.)
Postpartum cells
Cyanophilic parabasal or intermediate cells with a prominent border
Differential Diagnosis

• BV
• **STIs:** Trichomoniasis, Herpes, etc.
• Precancers

• **Vulvar Dermatoses:**
  • Lichen sclerosis
  • Lichen simplex chronicus
  • Lichen planus
  • Irritant, allergen, eczema, etc.
Rule out Dermatoses: LSC, LS, LP
VVA, GSM Treatments: Low Dose Rx for VVA Vaginal or Oral (NEW-Ospemifene)

- Pt preference, symptoms, safety, efficacy, impact decision to treat

- DO NOT use ORAL ESTROGEN for VVA symptoms only!!!
Estrogen- Local Vaginal Options: Minimal Systemic Absorption so Progestin NOT NEEDED !!!

Daily for 2-4 weeks, then twice weekly PRN

- **Vaginal estrogen creams**: 0.5-2 gms pv at bedtime
  - Conjugated Equine Estrogen /CEE (Premarin)
  - Estradiol (Estrace)
- **Estradiol vaginal tablets** (Vagifem): 10 mcg dose
  - If dry atrophy, or introital dyspareunia, less effective?
- **Vaginal estradiol ring** (Estring): every 3 months
  - Effective, convenient, may help OAB as pessary
- **NEW**: Vaginal estrogen inserts: (Imvexxy)
- **Risk of secondary yeast, approx. 50% !!!**
NEW: Ospemifene (Osphena)

- Non-estrogen, SERM, agonist to vulvar/vagina
- For Mod-Severe Dyspareunia assoc w VVA
- Oral 60 mg tablet
- Daily with food
- Similar efficacy to estrogen, over 4-12 weeks
- Avoid: Current cancer, CVD, stroke
- Side effects: Hot flashes, > vaginal discharge
- Breast (unclear, no human studies yet)
- Bone effects (appears protective)
NEW: Mona Lisa Touch

- Laser
- 3 procedures, yearly
- Re-epithelializes vaginal epithelium

- Expensive $$$
- Insurance coverage- plan specific

- Unclear: long term safety?
- NEW FDA WARNING: DO NOT RECOMMEND !!!
NEW: DHEA (Intrarosa, Prasterone) for Post-Menopausal VVA, GSM

• Daily use
• Dosing 0.05% (6.5% ovules) vaginal at bedtime
• Converted intracellularly into estrogen!
• BUT: Little to no rise in estradiol serum levels
• Option- if history of breast cancer!

FDA. FDA approves Intrarosa for postmenopausal women experiencing pain during sex. 2016 Nov 17; (epub:. http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm529641.htm

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Sexual Counseling: FUN
Complex, Individual, Time-consuming

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Sexual Counseling: Complex, Individualized

• Regular SEX, Sleep, Lifestyle!
• Lubricants: Poise, Sliquid
• Pelvic Physical Therapy (PT) APTA.org
• Vibrators: Middlesex.MD
• Dilators
• Romance!
• Orgasm before intercourse

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• Only **supra-physiologic** levels incr. libido!

• Investigators randomized post-hysterectomy menopausal women (mean total and free testosterone levels, 13.0 ng/dL and 2.2 pg/mL, respectively [below the range for healthy premenopausal women]) to 12 weeks of transdermal estradiol (0.05 mg daily) followed by 24 weekly intramuscular injections of placebo or testosterone enanthate at doses of 3.0 mg, 6.0mg, 12.5mg, or **25.0 mg** while continuing transdermal estrogen. N=62

• Need long term safety data!

• **MEANWHILE:** Enc **SLEEP**, healthy lifestyle

Huang G et al. Testosterone dose-response relationships in hysterectomized women with or without oophorectomy: Effects on sexual function, body composition, muscle performance and physical function in a randomized trial. Menopause 2014 Jun; 21:612. (http://dx.doi.org/10.1097/GME.0000000000000093) - See more at: http://www.jwatch.org/na35167/2014/07/14/exogenous-testosterones-effects-menopausal-women-matter?query=etoc_jwwomen#sthash.8hQ05kqb.dpuf
NEW: Flibanserin
Female “Viagra”

• FDA approved 2015
• Centrally mediating
• Oral: Taken daily
• Only 10% more effective than placebo
• Does NOT help all women
• Controversial
• NO ETOH
Abnormal Vaginal Bleeding: Post-menopausal

• ANY Vaginal bleeding 12 months after FMP*
  Spotting, 1 time, or 1 drop blood!
  NEW research: 9% have endometrial cancer

REFER, Mandatory Workup:
• Transvaginal ultrasound (Must do with EMB)
• Endometrial biopsy (EMB): > 5 mm Endom. stripe

*LMP = FMP = final menstrual period
Resources:
“Menopro” App

• App for handheld devices

2017 Clinical Practice Guidelines for the Management of Menopausal Women
North American Menopause Society (NAMS).

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Menopause Update: Summary

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Thank You and Good Luck! Questions Welcome

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References


References


