Management of Perimenopause and Menopause Symptoms

When I asked for a smoking hot body, this is NOT what I had in mind!!

Amy Tipp
APRN-NP, WHNP-BC

Today’s Objectives

At the end of this session you will be able to:

- Differentiate between perimenopause and menopause signs and symptoms
- Explain the different treatment options for perimenopausal women
- Describe treatments for women going through menopause
Signs and Symptoms
A woman’s personal sauna
Definitions

Perimenopause -

The period of a woman's life when physiological changes occur that begin the transition to menopause

Signs and Symptoms

**PERIMENOPAUSE**

- Heavy/irregular bleeding
- Estradiol decreases
- Hair loss/hair growth
- Decline in fertility
- Increasing episodes of amenorrhea
Definitions

Menopause -

Recognized as 12 consecutive months of amenorrhea

Signs and Symptoms

<table>
<thead>
<tr>
<th>MENOPAUSE</th>
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<tr>
<td>• Vulvovaginal changes</td>
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<td>• Weight gain</td>
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<tr>
<td>• Genitourinary symptoms</td>
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<tr>
<td>• Headache</td>
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<td>• Hair loss/ excessive hair growth</td>
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<tr>
<td>• Thin skin/loss of elasticity/collagen/ more wrinkles</td>
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<td>• Poor concentration/poor memory/trouble multitasking</td>
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Committee Opinions
Everyone is entitled to my opinion

Position Statements

• The American College of Obstetricians and Gynecologists (ACOG)
• The United States Preventative Services Task Force (USPSTF)
• The North American Menopause Society (NAMS)
THE AMERICAN COLLEGE OF OBSTETRICIANS AND GYNECOLOGISTS (ACOG)

- Menopausal therapy should not be used for the prevention of coronary heart disease
- Women in early menopause are at low risk of adverse cardiovascular outcomes
- Should be considered for the use of estrogen therapy or conjugated equine estrogen

THE UNITED STATES PREVENTIVE SERVICES TASK FORCE (USPSTF)

- Recommends against the use of combined estrogen and progesterone for prevention of chronic conditions
- Recommends against the use of estrogen alone for the prevention of chronic conditions
Position Statements

THE NORTH AMERICAN MENOPAUSE SOCIETY (NAMS)

- **Hormone Therapy (HT)**
  - Most effective for vasomotor symptoms (VMS) and genitourinary syndrome of menopause (GSM)
  - Prevents bone loss and fractures
- **Non-hormonal management**
  - Utilize for VMS when hormone therapy is not an option
  - Consider cost, time, effort involved, adverse effects, lack of long-term studies and interactions with medications

Women’s Health Initiative (WHI)

- **Sponsored by**
  - National Institute of Health (NIH)
  - National Heart, Lung and Blood Institute (NHLBI)
- **161,808 women aged 50 – 79**
- **Two major parts**
  - Clinical
  - Observational
Women’s Health Initiative (WHI)

- Clinical Trial
  - Enrolled 68,132 women in one of three prevention strategies
    - Dietary Modification Trial
    - Calcium/Vitamin D Trial
    - Hormone Therapy Trial

Women’s Health Initiative (WHI)

ESTROGEN + PROGESTIN COMBINATION THERAPY - FIRST ARM

- 0.625 mg of conjugated equine estrogens plus 2.5 mg of medroxyprogesterone acetate daily
- Stopped early 2002 due to:
  - Increased risk of breast cancer
  - Increased risk of cardiovascular disease
  - More harm than benefit
Women’s Health Initiative (WHI)

ESTROGEN + PROGESTIN COMBINATION THERAPY - FIRST ARM (FOLLOWUP STUDY)

- 5.2 years for every 10,000 women
- Increased risk of
  - Breast cancer - 26%
  - Stroke - 41%
  - Coronary heart disease - 29%
  - Venous thromboembolism - 42%
- Increased benefit for
  - Colorectal cancer - 37%
  - Bone fractures - 37%
- Should not be used for prevention of CHD

Women’s Health Initiative (WHI)

ESTROGEN ONLY - SECOND ARM

- Estrogen only
  - Women had hysterectomy
  - 0.625 mg of conjugated equine estrogens daily
  - Stopped early in March 2004
**Women’s Health Initiative (WHI)**

**ESTROGEN ONLY - SECOND ARM (FOLLOWUP STUDY)**

- 6.8 years follow-up for every 10,000 women
- Increased risk of
  - Stroke - 39%
  - Venous thromboembolism - 47%
- Increased benefit for
  - Colorectal cancer - 37%
  - Bone fractures - 39%
- No difference in risk of
  - Coronary heart disease
  - Colorectal/total cancer
  - Deaths with uncertain effects in breast cancer

**OTHER FINDINGS:**

- Combination therapy had twice the rate of dementia
- Both types of therapy
  - Increased the risk of urinary incontinence
  - Worsened symptoms in patients already experiencing incontinence
- Quality of life on combination therapy showed no improvement
- Relief of vasomotor symptoms occurred in the majority in combination therapy
- Not to be used
  - To prevent coronary heart disease
  - In women with underlying heart disease
Perimenopausal Treatment Options
Just when you figured out PMS, along comes perimenopause...

"You need strong medicine to relieve your symptoms. I'm prescribing chocolate."
Perimenopausal Treatment Options

- Oral contraceptives
- Long acting reversible contraceptives (LARCS)

Oral Contraceptives

- Low estrogen combined oral contraceptives
- 20 mcg pill
- Contraindications: Smoking, hypertension, migraines
- Contraception remains very important until menopause can be determined
Long-Acting Reversible Contraception (LARCS)

IUD Nomenclature:

- TCu380A (US commercial name ParaGard)
- LNG 52/5 (US commercial names Mirena or Liletta)
- LNG 19.5/5 (US commercial name Kyleena)
- LNG 13.5/3 (US commercial name Skyla)

Menopause Treatment Options
Because there's no such thing as menopause insurance
Menopause Treatment Options

• Hormone Replacement Therapy
• Non-Hormonal Replacement Therapy

Warning:
Due to the influence of hormones
I could burst into tears or
kill you in the next 5 minutes.
Starting Hormone Replacement Therapy

THINGS TO CONSIDER

- Indications
- Contraindications
- Choosing a candidate
- Calculating risks

Starting Hormone Replacement Therapy

THINGS TO CONSIDER

- Routes/Dose/Side Effects
- Duration
- Monitoring/Stopping
- Special Issues: Bioidentical Hormone Replacement Treatment
Indication

CANDIDATES

• Healthy
• Symptomatic
• Within 10 years of menopause or <60 years old
• No history of
  – Breast cancer
  – Coronary heart disease
  – Previous venous thromboembolic event
  – Stroke
  – Active liver disease

Cardiovascular Risk Assessment

Note:
- This risk assessment is based on the Cox regression model of proportional hazards.
- Cardiovascular disease includes coronary disease, cerebrovascular disease, peripheral arterial disease, and nephrosclerosis.
- It may be applicable women who have a history of history of cardiovascular disease.
- BMI: risk factors for women, high-density lipoprotein.

References
Calculation Pearls:

THINGS TO REMEMBER ABOUT CALCULATING RISKS

• Formal CVD risk calculation is ideal approach
• May not be necessary in
  – Thin
  – Healthy
  – Non-hypertensive
  – Non-diabetic patient
• For patients with increased risk of VTE
  – Recommend transdermal estrogen with a progestin that has a neutral effect on coagulation (micronized progesterone)

Hormonal Treatment Options

• Estrogen/Progestin
• Conjugated estrogen/bazedoxifene
Estrogen

• Estrogen therapy remains the gold standard for relief, in particular, hot flashes
• All routes appear to be equally effective for symptom relief (and bone density) but metabolic effects differ
• Route: Most started on transdermal 17 beta estradiol
• Standard dosing of estrogen given daily
  – Conjugated estrogen 0.625 mg or its equivalent are adequate for symptomatic relief in the majority of women
**Progestin**

- Add oral micronized progesterone as first line
- All women with intact uterus need BOTH progestin + estrogen to prevent endometrial hyperplasia
- Women who had hysterectomy should not receive progestin
- Most well known studied synthetic progestin is medroxyprogesterone (MPA) 2.5 mg/day

**The first choice of progestin is natural micronized progesterone (200mg/day for 12 days/ month or 100 mg/day)**

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**Conjugated Estrogen/Bazedoxifene**

- Treatment available for vasomotor symptoms and osteoporosis prevention
- Potential candidates:
  - Women with moderate to severe hot flushes who have breast tenderness with standard estrogen progestin therapy
  - Women who cannot tolerate progestin therapy due to side effects
- Risk of VTE is increased with bazedoxifene
Non-Hormonal Treatment Options

- Anti-depressants
- Gabapentinoids/Anti-epileptics
- Alternative therapies

ANTI-DEPRESSANT

- SSRI
  - Paroxetine salt 7.5 mg/day
  - Paroxetine 10-25 mg/day
    ***Cannot use if patient is on tamoxifen
  - Escitalopram 10-20 mg/day
  - Citalopram 10-20 mg/day

- SNRI
  - Desvenlafaxine 100-150 mg/day
  - Venlafaxine 37.5-150 mg/day
Non-Hormonal Treatment Options

GABAPENTINOIDS/ANTI-EPILEPTICS

- Gabapentin 900-2,400 mg/day
- Pregabalin 150-300 mg/day
- Clonidine 0.1 mg twice daily

Other Non-Hormonal Treatment Options

ALTERNATIVE THERAPIES

- Lifestyle changes
  - Cooling techniques
  - Avoiding triggers
  - Exercise
  - Yoga
  - Weight Loss
Other Non-Hormonal Treatment Options

ALTERNATIVE THERAPIES

• Mind/Body techniques
  – Cognitive behavioral therapy (CBT)
  – Mindfulness based stress reduction
  – Paced respiration
  – Relaxation
  – Clinical hypnosis

• Dietary Management
  – Soy foods and soy extracts

• Supplements
  - Black cohosh
  - Crinum
  - Dioscorea
  - Dong quai
  - Evening primrose
  - Flaxseed
  - Ginseng
  - Hops
  - Maca
  - Omega-3 fatty acids
  - Pine bark
  - Pollen extract
  - Siberian rhubarb
  - Combination botanical remedies
Non-Hormonal Treatment Options

ALTERNATIVE THERAPIES

• Other treatments
  – Acupuncture
  – Stellate Ganglion Block
  – Calibration of neural oscillations
  – Chiropractic interventions

Compounded Bioidentical Hormone Therapy

• “Bioidentical hormone” technically refers to hormone with same molecular structure as hormone that is endogenously produced
• Popular culture
  – Custom compounded,
  – Multi hormone regimens (pills, gels, sublingual tabs or suppositories)
  – Dose adjustment based on hormone monitoring
• Not recommended
Compounded Bioidentical Hormone Therapy

- No large clinical trials on
  - Efficacy
  - Safety
  - Adverse effects
- Derived from soy and plant extracts and modified to be structurally identical to endogenous hormones
- No evidence for safety or efficacy when compared to available products for MHT
- Quality may be substandard

As A Last Resort

"Hormone replacement therapy will make you feel much better. I'm replacing your hormones with rainbows, sunshine and glitter."
Stopping Hormone Therapy

• 40 - 50% stop within one year of starting MHT with no assistance of provider
• 65 - 75% stop within two years of starting MHT with no assistance of provider
• Abrupt withdrawal of estrogen at any age may result in hot flashes and other symptoms
• Although tapering has not been proven to be more effective, it is suggested

Stopping Hormone Therapy

TAPERING RECOMMENDATIONS

• Decrease estrogen by one pill/week (6 pills/week for 2-6 weeks, then 5 pills/week for 2-4 weeks, etc.)
• Decrease progestin with same taper
• Women with severe, recurrent symptoms during or after a 3-6 month taper should go back on estrogen
• May try a much slower taper
  – Sometimes over year (six pills/week for 2 months, then 5 pills/week for 1 month, etc.)
Stopping Hormone Therapy

TAPERING RECOMMENDATIONS

• Transdermal preparations have variety of doses (0.1 mg, 0.075 mg, 0.05 mg, 0.0375 mg, 0.025 mg, 0.0114 mg)
• Gradual dose reduction
• Usually over 3-6 months
  – If unsuccessful, repeat taper over 1 year

Overall Recommendations

• Start with lowest dose first then titrate up as needed
• Onset is typically within 2 weeks
• VMS often improve over time
• No clear recommendations for efficacy of one non-hormonal prescription over another
• When withdrawing, non-hormonal therapy should be done over 1 – 2 weeks
Overall Recommendations

- Choice of therapy depends on
  - History
  - Co-administered medications
  - Co-existing mood disorders
  - Whether VMS are worse during day or night
  - Patient preference
- Re-evaluate therapy every 6 – 12 months

Clinical Pearls

- Estrogen is most effective for relief of menopausal symptoms
- Menopausal hormone therapy (E or E + P) is indicated for management of menopausal symptoms
- Long term use is no longer recommended
- Women being treated only for vulvovaginal atrophy should be treated with low-dose vaginal estrogen
  
  ***Must also be considered in breast cancer survivors as a quality of life issue***
Clinical Pearls

• Goal of MHT - relieve menopausal symptoms and provide management of vaginal atrophy
• Other symptoms that respond to estrogen therapy include
  – Mood/depression
  – Genitourinary syndrome of menopause
  – Sleep disturbance
• For symptomatic women in 50's reassure them the risk of complications for healthy, post menopausal women taking MHT for 5 years is very low

Clinical Pearls

• For healthy peri/menopausal women
  – Within 10 years of menopause or <60 years with moderate to severe s/s, MHT is treatment of choice
• Exceptions
  – Breast cancer
  – CHD
  – Previous venous thromboembolic event
  – Stroke
  – Active liver disease
• Route
  – Start transdermal
  – PO is ok
  – All are equally effective for hot flashes
**Clinical Pearls**

- If recurrent hot flashes occur after stopping estrogen
  - Try non-hormonal options
  - If symptoms persist restart MHT at lowest dose.
- Intact uterus
  - Use both estrogen + progestin to prevent endometrial hyperplasia and carcinoma
- Try micronized progesterone as first line progestin
- Do no use MHT for prevention of chronic disease, however, women who cannot tolerate other options for osteoporosis may be reasonable candidates

**Helpful Resources**

- MenoPro App
- NAMS.com
- GoodRx
Some Final Advice

Management of Perimenopause and Menopause Symptoms

Amy Tipp
APRN-NP, WHNP-BC
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