2022 Update on Management of the Menopausal Patient

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Disclosures

- I have no financial disclosures
- I have presented this topic both before and after menopause
- The presentation could have changed to reflect personal experiences, BUT
- I have always tried to present the facts without bias
Learning Objectives

- Define menopause and perimenopause
- Outline genitourinary vs vasomotor symptoms
- List benefits of estrogen and progestogen treatment in normal menopause
- Outline treatment of patients with premature ovarian insufficiency
Definitions

- **Menopause**—cessation of menses for 12 months
- **Average age** 51.5 years
- **Perimenopause**—three years before and two years after cessation of menses
- **Laboratory markers** can be wrong
  - FSH > 25 mIU/ml, estradiol < 50 pmol/L
Definitions

- Early menopause before age 45
- Premature ovarian insufficiency before age 40
  - May be surgical
- 20% have no symptoms, 20% have severe symptoms
Menopause

- Cluster of symptoms and health problems
- Need to address at wellness visit
- Provider may have to begin the conversation
Vasomotor Symptoms (VMS)

- Affect 80% of patients, may last up to 10 years
- Thermoregulatory zone in hypothalamus
- More common in African-Americans, less common in Asian-American population
VMS

- Affect patient’s quality of life
- Interferes with sleep
VMS Triggers

- Red wine
- Hot liquids
- Spicy foods
- Warm sleeping environment
- Long sleeved clothing
VMS Triggers

- No good literature to support
- Patients will refute that however
Genitourinary symptoms of menopause (GSM)

- Prior to 2014 referred to as vulvovaginal atrophy (VVA), atrophic vaginitis, or urogenital atrophy.
GSM

- Loss of lactobacillus or decrease in colonization when estrogen is lost
- Higher pH, change in bacteria
- More prone to UTI and vaginitis
- Urethral caruncle, stenosis, prolapse
GSM

- Vaginal dryness, itching
- Labial atrophy, prolapse, introital stenosis
- Irritation, pain with intercourse
- May have bleeding with intercourse
GSM

- Affects quality of life
- Interferes w/ sexual functioning and relationships
- Body image “feel old”
Other menopausal symptoms

- Mood swings
- Cognitive dysfunction
- Depression
- Resurgence of symptoms, worsened by sleep deprivation
- Musculoskeletal aching
Other menopausal changes

- Weight gain 5-8 lb.
- 50% of women of menopausal age are OBSESE
- Increased risk of metabolic syndrome in this population
- Even without weight gain, there is often a change in body appearance
- Fat distribution, change in abdominal girth
Other menopausal changes

- Tired
- Change in libido
Other health problems

- Osteoporosis
- Increase heart disease risk
- Cognitive changes
Treatment Options

Let’s discuss GSM treatment first
Treatment of GSM

- Topical estrogen at lowest dose to be effective
- Available in creams, vaginal tablets, patches
- No need for progestogen
- Endometrial surveillance not necessary unless bleeding develops
Vaginal estrogen for GSM

- Help reverse atrophic changes while minimizing systemic exposure
- Increase in the vaginal rugae
- Increase in the number of lactobacilli
- Does not alleviate VMS or reduce risk of osteoporosis
Other GSM rx--Prasterone

- A synthetic equivalent of DHEA available in vaginal tablet form
- Improves vaginal epithelial cells, vaginal pH, parabasal cells
- Improves vaginal symptoms
- Serum levels of estradiol and testosterone remain wnl
- Do not use in pts who had ER+ breast cancer or are on estrogen modulators (tamoxifen)
Other GSM rx--Ospemifene

- Selective estrogen receptor modulator
- Reduces severity of dyspareunia
- Beneficial effects for vaginal dryness and bone health
- Anti-estrogenic effects on breast tissue
Other GSM rx

- Lubricants—water based stains less, pH 4.5
- Hyaluronic acid
- Laser rx
- Pelvic floor exercises and dilators
GSM rx--breast cancer patients

- ER on tamoxifen, MAY consider low dose vaginal estrogen
- Triple negative breast cancer survivors may be candidates for vaginal estrogen
Treatment Options
Vasomotor Symptoms
Hormonal therapy is the most effective treatment for VMS AND the prevention of osteoporosis.

- First hormonal therapy was approved in 1942.
- Widely used 1960’s-1990’s.
VSM rx--nonhormonal prescription

- SSRI, SNRI low doses, monitor for SE such as weight gain, loss of libido
- Gabapentin taken at bedtime, low dose 300 mg
- Clonidine
- Pregabalin
VMS rx--soy

- Weak plant estrogens called isoflavones
- May have SERM-like properties or may stimulate breast tissue
- Large placebo effect in most studies
VMS rx--CAM

- Mind-body such as meditation, CBT, biofeedback
  - Less negative side effects
  - Seem to be safe treatment and should be considered
- Herbal supplements
  - Insufficient evidence to support use
- Acupuncture, reflexology
VMS rx--Black Cohosh

- Systematic review of 16 RCTs showed insufficient evidence to support the use for menopausal symptoms
- Combined with St. John’s Wort, there was some improvement in depression
Menopausal Hormone Therapy
What happened and what’s new?
Menopausal Hormone Therapy (MHT)

- Widely used 1960’s-1990’s
- The Women’s Health Initiative changed all that
- Now we must relook at the data
Women’s Health Initiative (WHI)

- Enrolled 160,000+ women ages 50-79 in a set of clinical controls
- Low fat diet
- Calcium and vitamin D
- Estrogen only if no uterus
- Estrogen and progestogen if uterus present
WHI

- Evaluating several points
- Heart disease
- Breast cancer
- Colorectal cancer
- Fractures
Conjugated equine estrogens (CEE) if no uterus
Cee and medroxyprogesterone (MPA) for pts w/ uterus
One of the questions was “Does hormone therapy help prevent coronary artery disease?”
WHI

- Terminated early after average 5.2 years
- Risks exceeded benefits in CEE/MPA arm of study
- FDA put black box warnings on ALL estrogen and progestogen products
WHI

- We changed our practices
- Our patients were scared
- Our patients’ health problems did not change
- New look at the data
MHT

- Risk differs depending on type, dose, duration of use,
- route of administration, timing of initiation,
- and whether progestogen is used.
MHT

- Treatment should be individualized
- Use the best available evidence to maximize benefits and minimize risks
- Periodic re-evaluation of benefits and risks
MHT--estrogens

- Oral estrogen products: conjugated equine estrogen or estradiol
- Transdermal products are estradiol
- Transdermal products may have lower risk of DVT
MHT-estrogens

- Contraindications
  - Blood clots
  - Liver disease
  - Breast cancer
  - High triglycerides
- Gallstones are a common side effect
MHT—oral estrogens

- Enjuvia (conjugated estrogen)
- Estrace (estradiol)
- Menest (esterified estrogen)
- Premarin (conjugated estrogen)
MHT—transdermal estrogens

- Alora
- Climara (once weekly)
- Minivelle
- Vivelle dot
MHT--progestogens

- Progestogens must be used in combination with oral or transdermal estrogens if there is an intact uterus to prevent endometrial hyperplasia or carcinoma.
MHT—oral progestogens

- Medroxyprogesterone acetate
- Micronized progesterone (Prometrium)
- Norethindrone
- Drospirenone
MHT—endometrial protection options

- Levonorgestrel IUD
- SERM may be used
- Duavee is conjugated estrogen/bazedoxifene combination
  - Currently not available
MHT--progestogen

- Combination estrogen/progestogen therapy can be cyclic or continuous
- Continuous often causes irregular bleeding followed by amenorrhea
- WHI showed no increased risk of mortality from breast cancer
MHT—oral combinations available

- Activella (estradiol/norethindrone acetate)
- Angliq (estradiol/drospirenone)
- Duavee (CEE/bazedoxifene) not available
- Femhrt (estradiol/norethindrone acetate)
MHT—oral combinations available

- Prefest (estradiol/norgestimate)
- Premphase (CEE/MPA)
- Prempro (CEE/MPA)
MHT—transdermal combinations

- Climara Pro (estradiol/levonorgestrel)
- Combipatch (estradiol/norethindrone acetate)
Premature ovarian insufficiency (POI)

- Hormone therapy recommended until at least the median age of menopause, about 52
- Observational studies suggest that benefits outweigh the risks for effects on bone, heart, cognition,
- GSM, sexual function and mood
- Decision to continue after age 52 will be individualized w/ patient
Other rx--bioidentical hormones

- Patients think these are safer
- Compounded products do not have FDA safety sheets
- Rely on salivary hormonal testing which has been shown to be unreliable
Other rx--androgens

- NO FDA approved testosterone for women
- Risk of cardiovascular disease and breast cancer unknown
- Acne, lipid and liver function abnormalities
But what are the recommendations?
USPSTF

- No beneficial effect of estrogen for prevention of cardiovascular disease
- Reduce risk of osteoporosis
- Mild reduction in diabetes
North American Menopause Society 2021 recommendations

- MHT is indicated for women for women > 45 years of age to manage menopausal and GSM symptoms
- MHT can also be considered in the management of perimenopausal or recently postmenopausal women with risk factors for OSTEOPOROSIS
Women younger than 60 or who are within 20 years of menopause onset and have no contraindications, the benefit-risk ratio is most favorable for treatment of bothersome VMS and for those at higher risk for bone loss or fracture.

If older than 60 or more than 10 years after menopause, there is higher absolute risk of coronary artery disease, stroke, dementia, thromboembolic event.
Other health problems
What do we know?
MHT and heart disease

- The WHI was looking at this question
- Problem was that many women were started on MHT years after menopause
- In fact 20% of those enrolled were 70-79 years old
- Potential increased risk in women >10 years after menopause
- HERS trial showed no increase in CV events in patients on MHT
MHT and breast cancer (WHI data)

- Use of CEE alone, compared w/ placebo—lower breast cancer incidence and lower breast cancer mortality
- CEE/MPA, compared w/ placebo, significantly higher breast cancer incidence (9 per 10,000 years of rx)
MHT and breast cancer (WHI data)

- Attributable risk less than 1 additional case per 1,000 users annually
  - That is less than risk of 2 glasses of wine/day, obesity, low physical activity on breast cancer risk
- No significant increase in breast cancer mortality
MHT and VTE

- Increased risk across all ages w/ CEE or CEE/MPA in WHI
- Transdermal has lower risk in observational studies
- Consider personal or family hx when making decision
Okay now when do we stop MHT?

- Individualize “appropriate dose for appropriate duration”
- Most would suggest 5-10 years of rx
- Some women will accept the risk and ask for longer rx
- “Shared decision making”
Interesting studies

- Melbourne midlife women’s study
- Penn ovarian aging study
- These studies enrolled women in their early 40’s and study symptoms and hormone levels yearly
Questions?