Case Study

Marion, a 52-year-old female veteran, presents to your office for evaluation of hot flashes. For the last year she has been experiencing 6-7 hot flashes per day and often wakes up at night drenched in sweat. She feels fatigued and irritable most of the time. She has not had her menses for the last year, and reports significant vaginal dryness.

Marion thinks that she might be going through “the change” and wonders how long she will feel this way.

Discussion Points

• Symptoms often start in the perimenopausal period and usually involve irregular menses and vasomotor symptoms
• Vasomotor symptoms peak within 2-4 years after menopause
• 75% of women report vasomotor flushes. New data shows they continue for ~10 years and 15% report severe flushes for >15 years.
• Patients can try conservative measures like dressing in layers; using small portable fans; avoiding spicy foods, caffeine, chocolate, and alcohol, especially red wine. A food diary may highlight specific foods that trigger vasomotor symptoms. Yoga and exercise might be helpful as well.

Case Study, continued

Marion says that she is desperate for some relief from hot flashes now. She is a lawyer, and experiencing hot flashes during court has become very embarrassing. She has tried dressing in layers, avoiding hot beverages, and keeping the room cool, but nothing seems to work.

Her best friend was recently started on “hormone therapy” by her doctor. She wants to know if you would prescribe this for her.
Q2: Which of the following outcomes compared to the placebo group?

A. Breast cancer
B. Stroke
C. CHD
D. Colon cancer

Discussion Points

- Women randomized to E+P therapy, compared to a placebo group, experienced lower rates of colorectal cancer and hip fracture. Number needed to treat (NNT) to prevent 1 colorectal cancer was 333; NNT to prevent 1 hip fracture was 400.
- Women in E+P group experienced higher rates of CHD, stroke, venous thromboembolic disease, and invasive breast cancer. Number needed to harm for venous thromboembolic disease was 105. Global Index was >1, indicating overall net harm associated with treatment.
- Women in the estrogen-only arm experienced more strokes and fewer hip fractures, compared to a placebo group. Global Index was equivalent between the two groups, indicating no net benefit of therapy.

Q3. What do you tell Marion about her risk for MI with combination E+P therapy?

A. She should avoid combination E+P therapy altogether, because it will substantially increase her risk for MI.
B. E+P therapy will increase her risk for MI now, but if she waits until she is 62 she can safely start it.
C. She should wait to start E+P therapy until she is later in menopause, because it seems to be safer then.
D. She should start E+P therapy now, as her baseline risk for MI is low.

Case Study, continued

Marion is a non-smoker and her only medical problem is hypertension, which is well-controlled with hydrochlorothiazide. She has never had any abnormal mammograms, breast biopsies, or gynecologic surgeries. Her mother had a heart attack at the age of 65, and Marion is worried about having one herself. She wonders if it will significantly increase her risk of MI if she starts HRT now.
Discussion Points

- Based on reanalysis of WHI data, as well as HERS data, the risk for MI is not increased in early menopause (<10 years).
- Risk for MI with E+P was primarily noted in older women, much more distant from the onset of menopause.

Case Study, continued

After discussing the pros and cons of HRT with you, Marion is very eager to start it. She has heard that HRT comes as a patch, a pill, and a vaginal cream. She wonders which is best for her.

Q4. Which of the following is true?

A. Oral HRT is more effective than vaginal or transdermal methods for relieving vasomotor symptoms
B. Transdermal hormone therapy is less likely to be associated with stroke and DVT than oral therapy
C. As compared to low dose HRT, higher doses of HRT are more effective for relieving hot flashes and just as safe
D. Once started, women should stay on HRT for at least 10 years to avoid the recurrence of any hot flashes

Discussion Points

- All routes of systemic therapy are equally effective
- Transdermal method is associated with decreased risk of stroke and VTE vs. oral route
- Use lowest effective dose to relieve symptoms: 0.625 mg per day or lower
- Continuous regimens are associated with fewer hot flashes during estrogen-free periods and eventually induce amenorrhea in most women
- Vaginal estrogen primarily has local effects only (exceptions are Femring or using topical estrogen >2x/week which achieves systemic levels). Because they act locally, will improve systemic symptoms, but will avoid systemic risks.

Case Study, continued

Marion starts using a combined estrogen + progestin patch and experiences tremendous relief in her symptoms. However, she returns to your office six months later and states that she now wants to discontinue her HRT, because her sister was just diagnosed with breast cancer. She has started black cohosh OTC, and wants to know if she should continue it. Is there anything else you can prescribe?
Q5. All of the following have been shown to be effective for reducing hot flashes EXCEPT:

A. Placebo
B. Wellbutrin
C. Gabapentin
D. Venlafaxine

Discussion Points

• ~30% of reduction in hot flashes with placebo
• Wellbutrin: Small pilot study did not show a reduction in hot flash frequency and/or severity beyond what would be expected with a placebo
• Gabapentin: Doses starting at 300mg qhs can be effective, particularly for night sweats. Goal may be 900mg qhs. Can consider bid dosing if patient is responding well.
• Venlafaxine: Antidepressant effect may take 4-8 weeks to peak, but hot flash relief may start in 1-2 weeks. Start at 37.5 – 75 mg per day. Side effects are greatest with 150mg dose, which may not have better efficacy for hot flashes.

Q6. What herbal therapies have been shown to be effective for treating menopausal hot flashes?

Discussion Points

• Though data are extremely limited regarding effective herbal remedies for menopause, black cohosh and phytoestrogens (soy) have shown mixed results.
• Of importance is determining that agents are safe for individuals and don’t interfere with other medications or increase risks (e.g., may want to avoid excess use of soy in women at risk for breast cancer).

Case Study, continued

After discussing the non-hormonal treatment options with you, Marion wants to start venlafaxine for her hot flashes. However, she is worried about her severe vaginal dryness coming back. Can you prescribe anything that will be effective?
Q6. All of the following would be effective treatment regimens for Marion EXCEPT?

A. 10mcg intravaginal estrogen ring (replaced every 3 months).
B. Intravaginal 25mcg estrogen tablet, used daily for 2 weeks and then twice per week.
C. Replens™ vaginal moisturizer applied daily every 3 days.
D. Astroglide™ vaginal lubricant applied prior to intercourse.

Discussion Points

• Vaginal moisturizer uses a bioadhesive delivery which improves vaginal epithelium – improvements are equivalent to intravaginal estrogen cream for all measure of vaginal epithelial cells, vaginal itching and irritation, dyspareunia
• Vaginal lubricants (e.g., Astroglide) make intercourse more comfortable, but provide no long-term benefit to the epithelium
• Can use water-based lubricants; some women use lubricants like olive oil (not evidence-based, but often recommended)