Midlife Mood Swings: Connecting Perimenopause and Mental Health

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Menopause: last menstrual period defined retroactively after 12 months with no menstrual period, average age 51

Perimenopause: also known as the menopause transition, generally starts 4-8 years prior to menopause, start marked by irregular menses, STRAW criteria are gold standard to define

Symptoms:

Vasomotor Symptoms: also known as hot flashes or hot flushes, up to 85% of perimenopausal women, treatment: hormone replacement therapy, paroxetine, other SSRI/SNRI (off label), gabapentin (off label) or pregabalin (off label)

Vaginal Dryness & Dyspareunia: Vulvovaginal atrophy related, may also be associated with narrowing and shortening of vagina, uterine prolapse, up to 60% of women, will not improve over time without treatment, treatment: over the counter lubrication, vaginal estrogen, selective estrogen receptor modulator Ospemifene

Insomnia: changes to sleep architecture with aging AND perimenopause, women 2x as likely to have insomnia than men, treatment: improved sleep hygiene, cognitive behavioral therapy for insomnia, melatonin, hypnotic medications, consider causes- related to vasomotor symptoms consider hormone replacement therapy, sleep apnea work up and treatment if indicated, restless leg syndrome treatment if indicated, treatment of underlying mood disorder or anxiety

Cognitive Issues nearly ¾ women report subjective cognitive and memory concerns in menopause transition, verbal memory appears most significantly impacted, organization, planning and concentration also potentially impacted. Studies mixed. Perimenopausal hormone therapy may be helpful but not when started after menopause. Unclear connection to long term risk for neurocognitive disorder (dementia). Treatment includes lifestyle modifications, adaptation strategies, anticholinesterase inhibitors (may slow vs treat in dementia) and possibly hormone replacement therapy prior to menopause

Mood Symptoms Significantly increased risk of mood and anxiety symptoms in menopause transition. Symptoms of depression or other mental health d/o overlap with many perimenopausal symptoms including sleep issues and cognitive issues. Other symptoms of depression include appetite changes, loss of interest in previously enjoyed activities, unwarranted feelings of guilt, hopelessness, sad or depressed mood, or suicidal thoughts. Treatments can include medications, psychotherapy, and lifestyle changes.
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October 3rd, 2020

CE Requirements
- I have no disclosures.
- Venlafaxine is in a group of drugs called serotonin-norepinephrine reuptake inhibitors (SNRIs) commonly used to treat major depressive disorder, anxiety, and panic disorder. I will discuss this common use in my presentation, and will also discuss the off-label use of venlafaxine to treat vasomotor symptoms.

- Hormon replacement therapy is FDA approved for vasomotor symptoms, but not for depressive symptoms. We will discuss data for and against use of HRT for depression in menopausal transition but will not review specific formulations.

Objectives
- Discuss perimenopause including the symptoms associated with the menopausal transition
- Describe the impact of perimenopause on depression, mood, sleep and cognition
- Identify treatment strategies for mental health in perimenopause

First: What is Menopause?
Last Menstrual Period
Defined after 12 months of amenorrhea in the menstrual period
Average age: 51

What is Perimenopause?
a time of physiological and psychological changes as women near reproductive senescence

Typically noted first by menstrual irregularity
STRAW Criteria
Stages for Reproductive Ageing in Women chart per menopause to define perimenopause
Hypo-Pituitary–Gonadal Axis

Symptoms typically 4–8 years before menopause

Symptoms

Vasomotor Symptoms
- Up to 85% of perimenopausal women
- Severity worsens as near menopause
- Average duration of 5 years
- Several theories on why

Vulvovaginal atrophy
- Urogenital tissue highly estrogen sensitive, fluctuating and low levels of E leaves these tissues fragile
- Up to 60% of women report
- Can benefit from vaginal estrogen

Cognitive Changes
- Verbal memory (word list learning and recall)
- Unclear if corresponds to increased risk for major neurocognitive disorder
  - Thought unlikely to worsen outside pattern with normal aging
  - Unlikely for cognitive function to return to premenopausal baseline
- Worse in early perimenopause
- Subjectively reported by 72% of women
- May be exacerbated by mood symptoms
** majors Disorder**

5 of the following sx for 2 weeks:
1. Depressed mood (feel sad, empty, worthless)
2. Markedly decreased interest in activities
3. Significant weight loss or gain
4. Insomnia or hypersomnia
5. Psychomotor changes
6. Fatigue or low energy
7. Feelings of worthlessness or guilt
8. Decrease in concentration
9. Suicidal thoughts

If suicidal thoughts present consider emergency hospitalization.

** Differences?**

**Perimenopausal Specific Symptoms**
- Low energy
- Recurrent crying
- Unbearable irritability
- Decreased self-esteem
- Fatigue
- Anxiety
- Mood swings
- Sleep disturbances
- Weight gain
- Loss of sexual interest
- Problems with memory and concentration

**Differential Diagnosis**
- Substance use disorder
- Adjustment disorder
- Bereavement
- Bipolar disorder
- General medical causes of depression
- Psychological distress
- Persistent depressive disorder
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Risk Factors
- negative life events
- unemployment
- higher BMI
- smoking
- younger age
- race
- other factors

3x Risk of developing depressive episodes with perinatal depression

Real-World Impacts
- changes to romantic relationship
- children moving out of home
- changes to career
- retirement or reduced hours
- caregiver to aging parents

Why?

Functional Impairment

Cost

Associated with worsening medical comorbidity
- insulin resistance
- osteoporois
- cardiovascular events
- immune compromise
- increased recovery time from medical events

Treatment Options

Psychotherapy
- Cognitive Behavioral Therapy
- Mindfulness Education
- Interpersonal therapy

Medications

- Selective Serotonin Reuptake Inhibitors
  - citalopram, escitalopram, fluoxetine, fluvoxamine, paroxetine, sertraline
- Serotonin Norepinephrine Reuptake Inhibitors
  - desvenlafaxine, venlafaxine, duloxetine
- Others
  - mirtazapine, bupropion, TCAs, trazodone

Hormone Therapy

- NOT FDA approved for depression but some studies demonstrate improvement in perimenopausal depression, NOT postmenopausal depression
Complementary and Alternative Medicine: Lifestyle Modifications

- Exercise
  - Low to moderate intensity exercise reduces depression in middle-aged women

- Diet Changes
  - Benefit to anti-inflammatory diet
  - Lactose, fiber, fruits and vegetables

- Sleep Hygiene
- Support Outreach

- Decreased/Cessation of Alcohol and Substance Use

Complementary and Alternative Medicine: Herbal and Dietary Supplements

- Most have no evidence in randomized control trials
- Providers should ask about use of herbal treatments
- May interact with medications or other substances
  - Can be dangerous: liver toxicity, bleeding, estrogenic properties which should not be used in some breast cancers

St. John’s Wort (Hypericum perforatum)
- Some evidence in mild and moderate depression (not perimenopause specific)
- Varying recommendations internationally as preparations not standardized

Melatonin
- Licensed short-term therapy for sleep
- Melatonin may help in menopause transition not indicated for depression, but may help as sleep can be driving factor, but studies have not shown significant benefit
- Concerns over quality control of preparations

Soybean isoflavones
- Some evidence for benefit in studies out of Asia but study design concerns

Case Example

A 40-year-old woman reports increased anxiety, especially at bedtime. She describes her menopausal symptoms as moderate, with occasional hot flashes, but the severity has increased over the past few months. She is interested in alternative therapy options to help manage her symptoms.

Questions?
References