menopause:

MENTAL HEALTH AS A VITAL SIGN

Karen Giblin
CEO
Red Hot Mamas

Mache Seibel, MD
Harvard Medical School
Beth Israel Deaconess
Medical Center

Verna Brooks McKenzie, MD Adjunct Professor Touro University Medical Imaging Program Mary Jane Minkin, MD
Clinical Professor
Dept of Obstetrics, Gynecology,
& Reprod Sci
Yale Medical School

Disclosures

Karen Giblin



Nothing to disclose

Verna Brooks McKenzie, MD



Women's Health Advisory Board Member for Astellas (July 2022-October 2022)

Mary Jane Minkin, MD



Consultant for Astellas, Therapeutics MD, Schaper and Brummer, and Pfizer

Mache Seibel, MD



Nothing to disclose

Christine Welniak (Editor) and Matthew Fleming (Program Planning) also have nothing to disclose. All relevant relationships listed above have been mitigated.

Learning Objectives

At the completion of this episode, you should be able to:

- Recognize the relationship between mental health issues and menopause
- Examine the effects of hormone therapy in women in various stages of menopause
- Analyze treatment strategies for women experiencing menopauserelated depression

Surgical Decision for BRCA 1+; Worried About Depression

"I am almost 39 and just found out I am BRCA 1+ and am in the midst of of a major decision about when to get an oophorectomy or hysterectomy (and potentially breast surgery).

I have suffered from depression most of my adult life and had a serious post-partum depression after the birth of my daughter three years ago....

I was wondering if you have any suggestions concerning estrogen vs. estrogen + progesterone vs. other options. I am concerned about spiraling into a further depression."

CASE 1 Treatment Considerations

- BRCA 1+ increases risk of ovarian cancer, breast cancer, and endometrial cancer^{1,2}
- Patient concerned about depression related to surgical menopause
 - History of depression, including serious post-partum depression
 - Currently taking sertraline and bupropion
- Early (surgical) menopause introduces other health risks
 - Vasomotor symptoms (VMS) usually more severe in younger women and following surgical menopause³
- Without hormone therapy, increased risk of osteoporosis, dementia, heart disease, and sleep disturbances^{4,5}

¹National Cancer Institute. BRCA gene mutations: cancer risk and genetic testing. November 19, 2020.

²de Jonge, MM, et al. JNCI J Natl Cancer Inst. 2021;113(9):djab036.

³Gallicchio L, et al. Fertil Steril. 2006;85(5):1432-40.

⁴Nash, Z. Best Pract Res Clin Obstet Gynaecol. 2022;81:61-68.

⁵Joffe H, et al. Semin Reprod Med. 2010;28(5):404-21.

Hormone Therapies¹

- Estrogen therapy (ET) could ameliorate depressive symptoms
 - In perimenopausal women, the effect of ET on depression can be similar to antidepressant therapy
 - ET may augment the effectiveness of antidepressant therapy
 - ET improves sleep, which has been shown to benefit mood
- Cardiovascular benefit for younger women
- Breast cancer with ET is rare
- In women with an intact uterus, natural progesterone or estrogen + bazedoxifene are alternatives to progestin therapy

CASE

Treatment Recommendations

- Oophorectomy + hysterectomy
 - Reduce risk of cancer, obviate need for progestin, which could have adverse effect on mood
- Estrogen therapy (ET)
 - Use the lowest dose that addresses patient's symptoms¹
 - Adjust dose to control hot flashes and sleep disruption
 - ET for most patients should continue until the average age of menopause
- Change SSRI for depression if necessary
 - Monitor patient's mood; she may do well on ET and on current SSRI, sertraline
- Diet, exercise, and sleep hygiene
 - All women should be counseled on nutrition, exercise, and sleep hygiene.

¹North American Menopause Society (NAMS) Advisory Panel. Menopause. 2022;29(7):767-794.

Menopausal Woman Lacking Zest

"I am embarrassed to talk to my GYN about the way I feel. Menopause has caused me to feel depressed and I am carrying a burden of shame because I feel this way. I heard about postmenopausal zest which I think is a lie leading woman down the wrong path because I certainly haven't experienced it. What should I do?"

Treatment Approaches^{1,2}

- Cognitive behavior therapy (CBT) and interpersonal psychotherapy (IPT) have the most evidence.
- Mental health (MH) referral adds support and address MH symptoms
- Self-reporting scales for both depression and anxiety
 - Patient Health Questionnaire (PHQ-9)
 - General Anxiety Disorder-7 (GAD-7)
- A family history of depression increases patient's depression risk
- Unaddressed, co-occurring anxiety symptoms can have negative emotional health consequences that persist for decades
- Supporting sleep, social rhythms and nutrition improves outcomes

¹Cyranowski JM. Practice considerations for behavioral therapies for depression and anxiety in midlife women. NAMS Practice Pearl. October 7, 2021. https://www.menopause.org/docs/default-source/professional/practice-pearl-cbt-for-depression.pdf

²Coryell W, et al. Br J Psychiatry 2012;200:210-215.

Treatment: Medications

- Primary goal is to address symptoms through the root cause
 - Difficult to know if depression is 2° to menopause or not
- Hormone Therapy (HT): Estrogen is optimally prescribed for women 50-59 or within 10 years of menopause onset¹
 - If HT used, patches might provide lowest risk
 - Will require estrogen + progesterone if woman has uterus
- HT can be combined with antidepressant
 - Many SSRIs and SNRIs used for vasomotor symptoms (VMS)²

7 Treatment Recommendations

- Take a detailed history
- Understand her past mental health history
- Ask patient what is most important to her
- Provide menopause education including expectations and options
- Begin with lifestyle changes (nutrition, exercise, sleep, stress)
- Determine if mental health referral is in order
- Discuss diagnostic and prescription treatment options

Unmotivated Postmenopausal Woman

"I have been feeling just lost and not myself since I had my last ovary and fallopian tubes removed in 2016....I was diagnosed with heart failure in the same year...I feel listless, lifeless, depressed and negative feelings just go on....I have hot flashes continuously but mostly I have been unmotivated to do anything. My doctor has had me on Zoloft but I haven't renewed it in more than a month. I am soon to be 58 and when I realize I just can't get a handle on this I traced it back to 2016 right after the surgery. Please suggest something to me."

General Recommendations: Mental Health & Menopause

- Treatment should be individualized using the best available evidence to maximize benefits and minimize risks
- Hormone therapy (HT) is the most effective treatment of VMS and genitourinary syndrome of menopause (GSM)
 - HT has been shown to prevent bone loss and fracture
 - The benefit-risk ratio appears less favorable for women > 60 years or 10 years from their last menstrual period (greater absolute risks of coronary heart disease, stroke, VTE and dementia)
 - HT is not recommended for use in women with a history of coronary heart disease, myocardial infarction, stroke, venous thromboembolism (VTE), or inherited high risk of thromboembolic disease, estrogen sensitive cancer (including breast cancer)

¹North American Menopause Society (NAMS) Advisory Panel. Menopause. 2022;29(7):767-794.

General Recommendations: Mental Health & Menopause (Cont.)

- Non-hormone treatment options should be considered for women with bothersome hot flashes with contraindications to HT and women who choose not to take HT
- FDA approved non-hormone treatment of moderate to severe VMS
 - Paroxetine mesylate 7.5 mg daily
 - Fezolinetant 45 mg daily (further evidence on mood is lacking)

Non-Hormone Treatment Options¹

- SSRIs/SNRIs shown to significantly reduce VMS in large double-blind randomize control trials of symptomatic women
 - Escitalopram, citalopram, venlafaxine, desvenlafaxine
- Commonly used non-hormone treatment options can also be considered
 - Gabapentin 300 mg three times daily (improves frequency and severity of VMS)
 - Oxybutynin 2.5 mg or 5 mg twice daily up to 15mg extended release daily (demonstrated to significantly improve VMS in postmenopausal women)
- Cognitive-behavior therapy (CBT)
 - Reduction in VMS and depressive symptoms
 - Goal helping patients understand and change patterns of dysfunctional thinking and behaviors that contribute to negative emotional states

3 Treatment Recommendations

- This patient is not a candidate for hormone therapy (heart failure)
- Patient could benefit from non-hormone therapy to treat her VMS
 - Might start with gabapentin, if not contraindicated, to see if she responds; gabapentin also helps with sleep disruption due to continuous hot flashes
- Patient could benefit from antidepressant
 - She stopped taking her SSRI (unknown reason)
 - Would inquire about her willingness to try another antidepressant paroxetine 7.5mg (effective in reducing frequency and severity of hot flashes)
- Encourage patient to follow a healthy diet and get regular exercise
- Mental health screening to assess severity of mood symptoms and refer for CBT
- Reevaluate with shared decision making to monitor her progress

49-Year-Old Woman Who is "Cranky"

"I am almost 49 who believes that I am in my perimenopausal stage. I feel exhausted all the time, a bit cranky and annoyed, low sex drive, achiness throughout my body, have changes in my period (still having one), and I feel very depressed."

5 Woman with Anxiety and Muscle Weakness

"Can morning anxiety that sets in 5-15 minutes after waking, combined with exhaustion, muscle weakness, fear of leaving the house and depression be perimenopause symptoms? If so, any ideas what is needed to best treat? Could cortisol levels be playing a role?"

6 Symptoms Symptoms

"Will antidepressants help my menopause symptoms? I am so frightened to take HRT but I need some relief from hot flashes, night sweats, and feeling irritable and depressed all the time."

7 African-American Woman Feeling Hopeless

"I am a 54-year-old African American woman who has took a turn for the worst when my menopause kicked in. I am taking estradiol pills .05 after 1 week and it seems to give me heavy bouts of depression. I already have high anxiety. What can I do to ease the mental part of this menopause because I feel hopeless."

R How Do You Dose HRT?

"How can you determine the correct dosage of HRT to help with mood swings and depression? Any advice?"

9 Postmenopausal Woman with Generalized Anxiety Disorder

"I am three years post menopausal. I have generalized anxiety disorder for which I had been taking Zoloft for the past 17 years with much success. Although 3 years ago I did experience a period of unexpected anxiety. Now 3 years later, my anxiety is at an all time high. Increased Zoloft to 100 mg with no success. Now weaning off Zoloft and trying Lexapro. I haven't felt myself for months now. Now my question is could my anxiety be hormonal? I am also very depressed."

${f 10}^{\text{CASE}}$ Women on HRT Needs More Assistance for Mood Issues

"Started HRT 7 weeks ago. Estradiol patch and then the addition of Prometrium one week ago for poor sleep. Anxiety, mood swings and depression were my top complaint. Sleep improved reduced but I feel it could be better. Would an increase in estradiol or Lexapro be the next best step? Lexapro had helped before during Covid as I assumed it was stress related to that time not perimenopause."

1 **1**

Postmenopausal Woman Feeling Shame

"I am embarrassed to talk to my GYN about the way I feel. I am 60 years old, and I have not had my period for 5 years. Menopause has caused me to feel depressed and I am carrying a burden of shame because I feel this way."

$\overset{\text{CASE}}{12}$ Postmenopausal Woman with History of Depression

"I am 53 and a recent test by my GYN shows that I have been through menopause, although I have not had any symptoms. I have a history of mood disorders and depression and take Lamical, Latuda and Effexor. I have an IUD and would like to have it removed but I am concerned that the lack of hormones will dysregulate my moods. I appreciate any advice."

13 Woman with Surgical Menopause

"I am a breast cancer survivor and recently had my ovaries removed as a part of my treatment. Since then, I have had anxiety, depression, heart palpitations and hot flashes. Please help as I am depressed."

14 Mood during Perimenopause

"Is it normal to feel nervous, insecure and depressed during perimenopause?"

15 Depression & VMS

"I am struggling with depression and hot flashes. Should I take antidepressants or take HRT? I have an appointment with my doctor this month."

16 Depression

"Will taking HRT help my psychological outlook as I am feeling miserably depressed?"