

The Epidemiology of Psychiatric Illness During Perimenopause

SELF-STUDY
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REPRODUCTIVE
– PSYCHIATRY –

Objectives

- To understand the epidemiology, clinical characteristics, and risk factors for the following during the menopausal transition:
 - Depressive disorders
 - Bipolar disorder
 - Insomnia
 - Anxiety disorders
 - Psychotic disorders



Case

Ms. B a 49 yo married female who presents for a follow-up visit with her psychiatrist.

Psychiatric History: notable for major depressive disorder that has been well controlled over the last few years. She also reports an increase in mood symptoms the week before the onset of menses typically.

Pertinent Reproductive History: last menstrual period was 2 months ago, and she started to develop hot flashes 2 months before that.



Case

Ms. B has a good friend who is also going through menopause. Her friend has had persistent depressive symptoms and Ms. B worries about her own risk for this. Although her affective disorder has been well controlled, Ms. B asks her psychiatrist whether she is at elevated risk for worsening during the menopausal transition.



Case

- Which stage is Ms. B in?
 - A. premenopause
 - B. perimenopause
 - C. menopause
 - D. postmenopause
 - E. None of the above



Case

- Which of the following are risk factors for depressive symptoms during perimenopause?
 - A. Prior history of depression
 - B. Older age at the onset of menopause
 - C. History of premenstrual mood symptoms
 - D. A and B
 - E. A and C
 - F. All of the above



Definitions

The female reproductive stages have been defined according to the 'Stages of Reproductive Aging Workshop' or STRAW criteria and include:

- Reproductive Phase (or premenopause)
- Menopausal Transition (or perimenopause)
- Postmenopause

**these stages may have less applicability in the case of surgical/medically induced reproductive changes



Definitions

Reproductive Stage or Premenopause:

- Time of reproductive fertility
- Menstrual cycles are usually regular and hormonal markers are normal
- Typically lasts from puberty until early 40s

Perimenopause:

- 3 or more months of reduced and irregular periods due to naturally waning estrogen
- typically occurs in the mid-40s, averaging about 4 years in length

menopause =
last menstrual
period

average age
~52

Postmenopause:

- Starts 12 months after last period
- Menopausal symptoms can persist in some cases even after this point

Menopausal Symptoms are typically most intense during this period and can include:

- Hot flashes/night sweats
- Vaginal dryness
- Urinary problems
- Discomfort with sex
- Fatigue
- Irritability/mood lability
- Depressed mood
- Cognitive changes

Some describe peri-menopause to include 1 year after the final period

Perimenopausal Depression: epidemiology

- The menopausal transition (or perimenopause) is a time of increased vulnerability for affective symptoms
 - Similar to the premenstrual or post-partum time



Perimenopausal Depression: epidemiology

- Cross-sectional studies showed 45-68% of women report depressive symptoms during the perimenopause
 - Compared to 28-31% of premenopausal women
 - Not optimally designed to evaluate question of timing of symptoms
- Longitudinal studies including the ***Study of Women's Health Across the Nation (SWAN)***, ***Seattle midlife Women's Health Study***, and the ***Penn Ovarian Aging Study (POAS)*** provide more evidence that the risk for depressive symptoms increases during perimenopause
 - Design of these studies (prospective cohort, longitudinal) better able to evaluate the association between perimenopause and risk for symptoms and to assess timing of greatest risk for symptoms
 - Most studies showed that the late perimenopause is the period of greatest risk, though this has been variable
 - The POAS showed that risk for depressive symptoms decreased after the final menstrual period



Depressive Symptoms vs Major Depressive Episode (MDE)

- Most commonly women experience 'sub-syndromal' depressive symptoms which do not constitute a full major depressive episode
- The risk of experiencing a MDE during the menopausal transition is less clear as some studies (SWAN) have demonstrated an increased risk and others (POAS) have not
- Women at highest risk for a MDE during the menopausal transition had a history of prior MDE (SWAN)
- First lifetime MDE during the menopausal transition is less common



Differential

- The differential for depressive symptoms during the menopausal transition should include:
 - Sub-syndromal depressive symptoms
 - Major depressive episode due to a history of or new onset affective illness (such as MDD or bipolar disorder)
 - Psychological distress
 - Bereavement
 - Adjustment disorder



Perimenopausal Depression: pathophysiology

- Greater variability in estradiol levels has been linked to depressive symptoms during perimenopause
 - These fluctuations may impact the neurotransmitters involved in the pathophysiology of affective exacerbations as well as the neuronal architecture
- Allopregnanolone fluctuations, which have been linked to risk of perinatal depression, have also been implicated in perimenopausal depression



Perimenopausal Depression and Vasomotor Symptoms

- Previously the '*domino theory*' was the prevailing theory for depression during perimenopause
- The domino theory postulated:

Vasomotor symptoms (VMS)



Sleep Disturbance



Depression



Perimenopausal Depression and Vasomotor Symptoms

- More recent research has shown that the relationship between depression and VMS is more complex
 - Several studies have supported that depressive symptoms are linked with vasomotor symptoms (SWAN), whereas other studies have found that MDE or MDD were more closely linked with VMS (POAS)
 - Depressive symptoms may precede the onset of vasomotor symptoms
 - Severe vasomotor symptoms are not necessarily associated with the onset of depressive symptoms
 - Nighttime hot flashes specifically have been linked to depressive symptoms independent of sleep disturbance



Perimenopausal Depression: risk factors

- There are several categories of risk factors for depressive symptoms and major depression during perimenopause:
 - Demographic
 - Psychosocial
 - Medical
 - Menopause related



Perimenopausal Depression: risk factors

Demographic:

| Depressive Symptoms | Major Depression |
|--------------------------------|--------------------------------|
| Younger age at menopause onset | Younger age at menopause onset |
| African-American Race | African-American Race |
| Lower education | |

*Adverse child events (ACE) linked more closely with major depression (including new onset) than depressive symptoms

Psychosocial:

| Depressive Symptoms | Major Depression |
|--|--|
| Lower social support | Lower social support |
| Stressful Life Event/Adverse Childhood Event | Stressful Life Event/Adverse Childhood Event |
| Financial strain | |

**Note: the absence of a risk factor in a specific category (such as financial strain and major depression) does not indicate a negative relationship, but that this factor was not as well studied



Perimenopausal Depression: risk factors

Menopause related:

| Depressive Symptoms | Major Depression |
|---|---|
| Vasomotor symptoms | Vasomotor Symptoms |
| Sleep disturbance (Note: this can occur even in the absence of hot flashes) | Sleep disturbance (Note: this can occur even in the absence of hot flashes) |
| Increased bother from vasomotor symptoms | |

**Note: the absence of a risk factor in a specific category does not indicate a negative relationship, but that this factor was not as well studied



Perimenopausal Depression: risk factors

Medical:

| Depressive Symptoms | Major Depression |
|---|---|
| Prior depression | Prior depression |
| History of perimenstrual or perinatal/post-partum mood symptoms | History of perimenstrual or perinatal/post-partum mood symptoms |
| Nulliparity | History of anxiety |
| Elevated BMI | Elevated BMI |
| Smoking | Smoking |
| | Chronic medical condition |



Perimenopausal Depression: clinical presentation

- [Link to Progressive Case Conference Video...](#)



Bipolar Disorder during Perimenopause

- Not as well studied (compared to depression)
- Women with bipolar disorder are at an increased risk for affective exacerbation during the menopausal transition, although research on this is limited
- Some studies have identified the late perimenopause and early postmenopause as the periods of highest risk for exacerbation
- Depressive episodes are the most common type of mood episode
- Exacerbations have not been correlated with specific hormone profiles



Insomnia and Sleep Disturbance during Perimenopause

- 30-60% of women experience sleep disturbance during perimenopause
- Sleep disruption may be present even in the absence of vasomotor symptoms
- The risk for primary sleep disorders such as obstructive sleep apnea is also increased during midlife



Insomnia and Sleep Disturbance continued..

- Perimenopausal related sleep disturbance is most often a ***sleep maintenance*** problem
 - Women most frequently report awakenings as the most common sleep disruption, and less often difficulty with sleep initiation



Anxiety Disorders during Perimenopause

- Anxiety during the menopausal transition has been linked with more significant vasomotor symptoms
- Anxiety during perimenopause has been linked to increased risk for cardiovascular disease, though the mechanism underlying this is unclear
- Prior research has shown that women with panic disorder are at increased risk for exacerbations during this period



Psychotic Disorders during Perimenopause

- Women with schizophrenia may be at increased risk for exacerbation during the menopausal transition
- Prior history of hormonal sensitivity (history of premenstrual or post-partum exacerbation) is an indicator of potential vulnerability during the perimenopause
- Prior research explored whether estrogen replacement could be an effective treatment for women with illness exacerbation (both for the psychotic and cognitive symptoms) and menopausal symptoms; these results have been variable and therefore psychiatric medications remain the mainstay of treatment



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