Objectives

- Define PMS & PMDD
- Review epidemiology surrounding these diagnoses
- Review diagnostic criteria
- Review therapeutic management options

Disclaimer

- These slides were created based on a review article written for AAFP published August 1st, 2016 by Dr. Hofmeister and Dr. Bodden

Case 1: CB

- 25 y/o female presents to your clinic with recurrent headaches and depression.
- What other questions might you ask her?

Case 1: CB (cont)

- Headache comes and goes for about 6 days
- Goes away a couple days after menses begin
- Band distribution-throbbing pain
- Ibuprofen does help somewhat
- No visual/auditory changes
- Depressed mood, not all of the time
- SIG E/CAPS overall positive maybe half of the month
- Further ROS reveals subjective bloating and weight gain

Case 1: CB Differential

- Depression
- Hypothyroidism
- PMDD
- Dysthymic Disorder
- Migraines
- Stress/Conversion Disorder
Premenstrual Disorders

Conditions consisting of psychiatric or somatic symptoms that occur during the luteal phase of the menstrual cycle, impact normal daily functioning, and resolve shortly after menstruation

- Psychiatry and OBGYN have overlapping but distinct diagnoses that qualify as premenstrual disorders

ACOG Definition

Premenstrual syndrome can be diagnosed if the patient reports at least one of the following affective and somatic symptoms during the 5 days before menses in each of the three prior menstrual cycles:

Affective
- Depression
- Angry outburst
- Irritability
- Anxiety
- Confusion
- Social Withdrawal

Somatic
- Breast tenderness or swelling
- Abdominal bloating
- Headache
- Joint or Muscle pain
- Weight gain
- Swelling of extremities

*these symptoms are relieved within 4 days of the onset of menses, without recurrence until at least cycle day 13. The symptoms are present in the absence of any pharmacologic therapy, hormone ingestion, or drug or alcohol use. The symptoms occur reproducibly during two cycles of prospective recording. The patient exhibits identifiable dysfunction in social, academic, or work performance.

APA Definition: DSM V Criteria (PMDD)

A. In the majority of menstrual cycles, at least five symptoms must be present in the final week before the onset of menses, start to improve within a few days after the onset of menses, and become minimal or absent in the week post-menses.

B. One (or more) of the following symptoms must be present:
   1. Marked affective lability (e.g., mood swings; feeling suddenly sad or tearful, or increased sensitivity to rejection).
   2. Marked irritability or anger or increased interpersonal conflicts.
   3. Marked depressed mood, feelings of hopelessness, or self-deprecating thoughts.
   4. Marked anxiety, tension, and/or feelings of being keyed up or on edge.

C. One (or more) of the following symptoms must additionally be present, to reach a total of five symptoms when combined with symptoms from Criterion B above:
   1. Decreased interest in usual activities (e.g., work, school, friends, hobbies).
   2. Subjective difficulty in concentration.
   3. Lethargy, easy fatigability, or marked lack of energy.
   4. Marked change in appetite; overeating; or specific food cravings.
   5. Hypersomnia or insomnia.
   6. A sense of being overwhelmed or out of control.
   7. Physical symptoms such as breast tenderness or swelling, joint or muscle pain, a sensation of “bloating,” or weight gain.

Note: The symptoms in Criteria A–C must have been met for most menstrual cycles that occurred in the preceding year.

D. The symptoms are associated with clinically significant distress or interference with work, school, usual social activities, or relationships with others (e.g., avoidance of social activities; decreased productivity and efficiency at work, school, or home).

E. The disturbance is not merely an exacerbation of the symptoms of another disorder, such as major depressive disorder, panic disorder, persistent depressive disorder (dysthymia), or a personality disorder (although it may co-occur with any of these disorders).

F. Criterion A should be confirmed by prospective daily ratings during at least two symptomatic cycles. (Note: The diagnosis may be made provisionally prior to this confirmation.)

G. The symptoms are not attributable to the physiological effects of a substance (e.g., a drug of abuse, a medication, other treatment) or another medical condition (e.g., hyperthyroidism).

Epidemiology

- 80% of women report at least one physical or psychiatric symptom during the luteal phase of their menstrual cycle, but for most this does not cause significant impairment in daily life
- Review studies
- Weight gain and increase in stress = more likely diagnosis of PMS
- PMDD prevalence between 1.3-5.3%

Etiology

- Poorly understood
- Some studies suggest cyclic changes in estrogen/progesterone may trigger symptoms
- Estrogen suppression with GnRH analogues has been shown to improve symptoms
- Higher levels of estrogen/progesterone dose not lead to higher rates of PMS or PMDD
- Estrogen/progesterone can alter Serotonin, GABA DA and RAAS
- Twin studies

Diagnosis

- TIMING, TIMING, TIMING!
- Symptoms occur during the luteal phase and resolve shortly after menstruation
- Depression or anxiety or other conditions may worsen during the luteal phase, but lack the symptom-free mid-follicular period
- Physical exam findings?
- Labwork?
Diagnosis

- Retrospectively, patients overestimate the cyclical nature of their symptoms
- Prospective Questionnaires most accurate
- The Daily Record of Severity of Problems (DRSP) is a reliable and valid tool that can be used to diagnose PMS or PMDD
- It is a daily log of symptoms that correlate with the diagnostic criteria for PMS and PMDD
- The patient rates their symptoms through at least 2 menstrual cycles (exception can be made)
- See handout for DRSP details

DRSP

Treatment

- Focus of relief of distressing physical/psychiatric symptoms
- Several pharmacologic options
- Physicians can attempt to tailor meds to fit each patient’s case
  - High placebo response occurs
  - Tailor therapy based on patient tolerance

SSRIs

- FDA Approved in the US for primary treatment
- Sertraline
- Paroxetine
- Fluoxetine
- Fluvoxamine
- Citalopram
- Escitalopram
- Considered first line for severe symptoms
- Cochrane Review
- Can administer continuously or just luteal phase

SSRIs (cont)

- Main Side effects: nausea, asthenia, fatigue, sexual dysfunction
- All doses appeared effective for psychiatric symptoms
- Moderate-high doses needed for relief of physical symptoms
- Bupropion not found to be helpful

SNRIs

- Venlafaxine used off-label mostly for women with predominantly psychological symptoms of PMDD at low doses (90mg) daily.
- Effect achieved over 3-4 weeks (short time) and sustained through subsequent cycles
Quetiapine 17

- Studied as adjunct treatment to SSRI or SNRI in patients who did not respond to single agent alone
- Reduced mood lability, anxiety and irritability during luteal phase

Oral Contraceptives (OCPs) 18,19

- Studies suggest benefit—frequently used in the US
- Improve physical and psychiatric symptoms (30-50%)
- Higher placebo response found in women with PMDD than PMS
  - Difference in baseline symptoms?
  - Continuous treatment may help the most for PMDD

Calcium Supplementation 21

- Cyclic changes in calcium levels noted in women with PMS and mood instability, mechanism unknown.
  - Review studies
  - 1000-1500mg calcium carbonate daily helps reduce depressive symptoms, appetite disturbances and fatigue

GnRH agonists 25,26

- International Society of Premenstrual Disorders gives consideration to this (eliminate the luteal phase and associated symptoms)
- Tried since the 1980s and are effective
  - Not practical for long-term use due to elevated cardiovascular risk and risk of osteoporosis with long-term use and side effects
  - Many women need hormone “add back” therapy to counter the hypoestrogenic side effects which can cause the PMS symptoms to return

Other Vitamin Supplements 23,24

- Low vitamin D levels not associated with risk of developing PMS
  - Further studies needed to support use in treatment of PMS or PMDD
- Not enough data to support use of B6, vitamin E or magnesium

OCPs + Drospirenone 20

- Separate Cochrane Review
  - 5 Trials, 1920 women
  - Reduced productivity impairment and impairment in social functioning for PMDD but not necessarily PMS
  - Take Home Message: you don't need Yaz.
Back to case CB

- She completed the DRSP and was found to have PMS, her symptoms were not severe enough to qualify for PMDD
- We considered using an SSRI since she had the significant depressive symptoms
- She is interested in getting pregnant soon so we did not want to use OCPs
- Opted for calcium supplementation (1500mg daily since she will likely get pregnant soon), gave her additional calcium and a prenatal vitamin
- Will see her back in a couple of months to review progress

Questions?

References