Premenstrual Syndrome

“Don’t mess with me!”

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Feb 2013
NO I DON'T HAVE

PMS
Case #1

- 27 yo female, h/o panic attacks, clean off meth x 5 years. C/o “crazy heart palpitations” memory loss, cramping, panic, +SOB, always right before her periods. **Resolve when menses starts**, but irregular.
- Broke up with previous boyfriend, job status – shaky, mother is ill.
- Obese, tachycardia, meets Rotterdam PCOS criteria
- x4000 calls x 3 in the first month.
- Anxiety – brother states she is “wigged out”
Case #2

- 47 yo Japanese-American physician, early menarche
- h/o irregular cycles, pre-menstrual sx: bloating and weight gain, depression/anxiety, hyperphagia (esp for red meat, carbs, caffeine), breast tenderness, low back pain. All which resolve by day 4 of cycle.
- Worsened by stress of medical training, q4 attending call...
- Occasional irritability.
  - All right, I said occasional!
Definition of PMS

- Recurrent, cyclic set of physical and behavioral symptoms that occur 7 – 14 days before the menstrual cycle.
- Troublesome enough to interfere with the woman’s life.
- Can affect 40% of menstruating women
  - Estimates range as high as 70-90% of women with 1+ sx
  - Most severe cases (2-5%) in women betw 25 -35.
- Complex interplay of hormonal and neurotransmitter factors that contribute to PMS
PMS Symptoms

- Fluid retention
- Neurologic
- Inflammatory
- Hormonal
- GI
PMS Symptoms

- **Fluid retention** - Water retention, weight gain, breast tenderness
- **Neurologic** - Irritability, depression, anxiety, fatigue, mood swings, headaches, lethargy, did I say mood swings?
- **Inflammatory** - Low back pain, joint pains
- **Hormonal** - Acne, appetite increase, low libido
- **GI** - Constipation or diarrhea, abdominal bloating
13 THINGS PMS STANDS FOR:

1. PASS MY SHOTGUN
2. PSYCHOTIC MOOD SWING
3. PERPETUAL MUNCHING SPREE
4. PUFFY MID-SECTION
5. PEOPLE MAKE me SICK
6. PROVIDE ME with SWEETS
7. PARDON MY SOBBING
8. PIMPLES MAY SURFACE
9. PASS MY SWEATS
10. PISSY MOOD SYNDROME
11. POOR MEN SUCK
12. PACK MY STUFF

&&& MY FAVORITE ONE

13. POTENTIAL MURDER SUSPECT
Definition of PMDD

Premenstrual Dysphoric Disorder – at least 5 of the following symptoms, must OCCUR CYCLICALLY, and serious enough to interfere with normal activities.

1. Sadness, or hopelessness, possible suicidal ideation
2. Anxiety
3. Mood swings marked by periods of teariness
4. Persistent irritability or anger
Definition of PMDD

5. Disinterest in daily activities and relationships
6. Trouble concentrating
7. Fatigue or low energy
8. Food cravings or binging
9. Sleep disturbances
10. Feeling out of control
11. Physical symptoms – bloating, breast tenderness, headaches, joint and/or muscle pains.
*Problems with dx of PMDD

- Vast number of other syndromes overlap with this.
  - Sx may point to other underlying psych diagnoses which are EXACERBATED by cyclic changes.

- While the severity of these PMS symptoms was known for years, not ‘officially’ a diagnosis until 1994.
  - Interesting that Eli Lilly presented fluoxetine (Prozac®) in 1974. Q: How long is FDA patent?
  - Also interesting that Sarafem® (aka fluoxetine) came out in 1994...
  - Things that make you go Hmm...
Differential Dx: Rule these out

- Major depression, Mood disorders
- Thyroid dysfunction
- Early menopause
- Eating disorders/ substance abuse

PMS is distinguished from chronic psychological disorders by a symptom-free period less than or equal to one week during the follicular phase (after menses/before ovulation) of each menstrual cycle.

- 75% women seeing specialists for PMS, dx’d with mood d/o

Theory: Progesterone

- Progesterone
  - Progesterone deficiency theory – first postulated by Dr. Katherina Dalton in 1950’s.
  - Relatively low progesterone in luteal phase
  - Progesterone is metabolized in brain to $3\alpha 5\alpha$-THP, which increases GABA, and calming effect.
  - 2012 Cochrane Review – only 2 trials qualified, benefits of progesterone inconclusive.

Cochrane Database Syst Rev. 2012 Mar 14;3:CD003415
Theory: Estrogen

- Estrogen staying too high during luteal phase (relative P deficiency)
  - Correlated to PMS severity: depression, anxiety, tension, swelling and headaches.

- (Rare type of PMS with LOW luteal phase E = severe depression)

- Higher estrogen states – seen with excess adipose, poor liver elimination, B vitamin deficiencies. Also dysfunctioning corpus luteum not pumping out enough P

Levitt A. PMS Chapter, CAM Secrets, 2002.
Theory: Prolactin & Aldosterone

- **Prolactin** –
  - Levels peak at ovulation, remain relatively high during luteal phase
  - Assoc with menstrual irregularities, depression, hostility, breast tenderness, and decreased libido.
  - Some say ~ 62% women with menstrual d/o’s have elevated PRL.

- **Aldosterone**
  - Also high after ovulation, and during luteal phase
  - May cause edema, breast swelling, bloating, HA

Theory: Co-factors

- Vitamin B-6 (pyridoxine)
  - Required for metabolism of fats, protein, carbs
  - Needed in rxn of 5-HTP and dopamine
  - B-6 deficiency $\Rightarrow$ low levels of serotonin, dopamine and higher levels of prolactin
  - Therefore, more depression and mood changes

- Magnesium
  - Lower RBC-magnesium noted in one study, $n = 105$ women with PMS cp to controls.

Ann Clin Biochem. 1986 Nov;23 (Pt 6):667-70
Theory: Others

- Inflammatory Prostaglandins (PG’s)
  - Assoc. with breast tenderness, fluid retention, abd cramping, headaches, irritability and depression.
  - Pts with PMS with these sx respond to PG inhibition.
    - NSAIDS, omega-3, and EPO.
- “Stress” – most any life stressor, poor sleep, illness, known mood disorder, also cultural and societal attitudes affect PMS.
But not just ovaries alone...
Biochemistry of steroid sex hormones

Cholesterol

↓

Pregnenolone → x → DHEA

17, 20 desmolase

17, 20 desmolase

Progesterone

↓

Adrenal only

3 steps to

Adrenal & Ovary

to testosterone

and estradiol.

↓

Aldosterone

2 steps to

Cortisol

AAEM 2011  McDaniel - Ovaries
Treatment of PMS

Exercise!

• Women who exercise note improvement in ALL sx of PMS
• Frequency: At least 3x/week, aerobic appears more effective
• Intensity also important – moderate is best.
• Diminishes negative mood sx, bloating, irritability

*J Psychosom Res.* 1994; 38:183-192
Supplements

Calcium
- Prospective, RCT done on n = 466 women. Calcium carbonate 1200 mg/day significantly reduced PMS symptom scores on validated scale.

Magnesium
- Helpful for reducing dysmenorrhea/cramping; unclear benefits for PMS
- Dose: 200 – 600 mg/day
- Helps to counteract calcium

Am J Obstet Gynecol. 1998; 179:444-452
Cochrane Database Syst Rev 2002; 2:CD002124
Supplements

- Vitamin B6
  - Used in more than 100 enzyme rxns, esp. serotonin, DA, NE.
  - Syst Rev: Small studies, patient with mixed dx’s, but OR = 1.57 in favor of using B6 (CI 1.4 – 1.77)
  - Depressive sx OR 2.12 (CI 1.80 – 2.48)
  - *LIMIT dose to 50 mg/day.

BMJ. 1999; 318:1375-1381
Chaste Tree Berry Extract  
(Vitex agnus-castus)

- Mech: Reduces PRL, increase progesterone, bind opiate receptors
- RCT on chaste tree – n = 170 women with PMS.
  - 20 mg extract x 3 months
  - Signif reduction in irritability, mood, headache, breast fullness.
  - 52% PMS sx reduction cp to 26% controls

- Another RCT, n = 217 women with mod-severe PMS
  - 40 mg x 4 months
  - Signif sx reduction

BMJ. 2001; 322:134-137.  
GLA: Evening Primrose Oil
(Oenothera biennis): Studies inconclusive

Omega 6 Fatty Acid
(Linoleic Acid)

Δ6-Desaturase

Gamma-linolenic acid
(GLA)
Evening Primrose Oil
Borage Oil
Black Current Oil

Δ5-Desaturase

Arachidonic Acid

Prostaglandins
PGE1, PGE3
(Favorable)

Leukotrienes

Eicosapentaenoic Acid
(EPA)

COX

Prostaglandins

DOCOSAHEXAENOIC ACID
(DHA)

Less Inflammatory
Leukotrienes

Delta-5-Desaturase

Linoleic Acid

Omega 3 Fatty Acids
(alpha-linolenic acid)

Leukotrienes

Lipoxygenase

Cyclo-oxygenase
(COX)

Prostaglandins (PGE2)
Inflammatory
SSRI’s for PMS

- Syst Review of 29 studies
- Fluoxetine, sertraline, paroxetine, citalopram
- Approx 3000 women
- Treatment with SSRI: OR 0.40 (CI = 0.31 – 0.51)
- CONTINUOUS regimens fared better (versus luteal only).
- No SSRI was more favorable than another.

Vitamin “I”

- Ibuprofen – Just do it.
  - Anti-inflammatory, inexpensive
- Midol®?
  - Acetaminophen 500 mg. Pain reliever
  - Caffeine 60 mg. Diuretic
  - Pyrilamine maleate 15 mg. Antihistamine
  - “Extended release” = 220 mg naproxen.
Limit alcohol and avoid drugs of abuse

Exercise! Goal: At least 3x/week x 30 minutes
  - Aerobic exercise
  - Other forms: ___________________

I WILL DO __________________ by __________.
PMS Prescription Pad

Nutrition

- Reduce: Salt, refined sugar, caffeine, esp 10 days before menses.
- Eat a well-balanced diet that is high in fiber; aim for 25 grams of fiber daily
- Ensure that your diet provides:
  - 1000 – 1200 mg calcium (citrate)
  - 400 mg magnesium (citrate)
  - OR choose to supplement these

I WILL ____________________________________________________________.
PMS Prescription Pad

- **Supplement:**
  - Vitamin B6 50 – 100 mg/day
  - Omega 3 fish oils – 1000 – 2000 mg EPA + DHA/day

- **Stress management**
  - Relaxation technique: _____________________________
  - Counseling _____________________________
  - Sleep _____________________________
Other specific treatments:
- Chaste tree berry extract (Vitex) 20 – 40 mg/day of standardized extract.
- Evening primrose oil: 1.5 grams twice daily
- SSRI _____________________
- NSAID of choice prn ____________________
- IM Clinic referral ______________________________

Signed: ________________________________

Patient  Physician/ Provider
Case #1 – 27 yo woman with severe PMDD, panic, palpitation, PCOS.

- Labs (routine): normal
- Started on Seasonique, which regulated and reduced cycles.
- SSRI – sertraline 100 mg/day
- B vitamin complex, Calcium 1200 mg/day
- Naprosyn, and trazodone prn
- LOST 30 #, started new job, dramatic sx reduction, has great outlook on life.
Case #2 .... Hmm

- Exercise made a huge difference
- Regular ingestion of omega-3’s as anti-inflammatory
- Meditation
- Still get cyclic food cravings
- Testing hormones now...
- Improving HPA axis via regular, more consistent sleep
  >7.5 hours qhs, computer off at 9:30 pm, catching morning light. (rebalance melatonin/cortisol cycles)