PMDD

PREMENSTUAL DYSPHORIC DISORDER: Modern Day “Moon Sickness”?

Linda DiRaimondo, MD
Madison, WI
May 2005

Menarche – The First Period

- Very powerful psychological, sociological, and physiological event in a woman's life.
- Rite of passage.
- Entrance into reproductive years. (Rosenthal, 2003)
- The average woman has 459 menstrual cycles and multiple factors (biological, psychological, societal) will effect the quality of these cycles.

Risk of Negative Experience

- Misunderstanding for young women – shame, fear, anxiety, depression at onset of periods.
- Pain and cramping.
- Sexual partner repulsed by flow.
- Mythology – *“the curse”*
- Prior to 20th century, menstruation seen as mysterious and evil with premenstrual emotions branded as “hysteria.”

(Rosenthal, 2003.)

The Moon Cycle

- The menstrual cycle is the only human life event that consistently corresponds to the lunar calendar (every 28 days.)
- The word *menstrual* derived from Latin *mens* meaning “month” from root word *moon*. Greek word *mene* = “moon” and *menstruation* = “moon change”.
- In French, menstruation called *le moment de la lune*, “the moment of the moon.”
- “Moon sickness” to the Maori, natives of New Zealand.
- Countless other cultures link moon & menstruation.
- Women living together will often synchronize cycles.

(Rosenthal, 2003.)

The “Normal” Cycle

- “A symphony of hormones.”
- Hypothalamus secretes FSH-RF (Follicle-stimulating hormone releasing factor)
- Pituitary releases FSH
- FSH triggers 10 to 20 follicles in ovary to grow.
- As follicles grow, they secrete increasing amounts of estrogen.
- Estrogen causes lining of uterus to grow/proliferate (proliferatory phase.)
- Egg matures in follicle causing burst of progesterone & estrogen.
- Hypothalamus triggered to secrete more FSH-RF & LH-RF (leutinizing hormone releasing factor) causing the pituitary to release FSH and LH simultaneously.
- FSH and LH levels peak signally follicle to release egg – ovulation.
- LH influences the follicle to change to corpus luteum which secretes decreasing estrogen and increasing progestrone (luteal phase.) Progesterone stimulates the uterus to secrete fluids that nourish the egg.
- If fertilization (pregnancy) does not occur, progesterone levels drop leading to the shedding of the uterine lining – menstruation. (Rosenthal, 2003)

When is the cycle “abnormal”?

- Presence of unpleasant, disturbing emotional and physical symptoms before monthly period.
- Symptoms disrupt life and interfere with usual activities and relationships with others.
- Symptoms go away when flow begins or shortly thereafter, only to return before next period.

(Endicott)

PMDD – Historical Perspective

- Hippocrates (460-377 B.C.) commented on women with suicidal thoughts and other premenstrual symptoms.
- In 1931 the term ***premenstrual tension*** first appeared and later evolved into ***premenstrual syndrome*** or PMS.
- In the late 1980s the more severe symptoms of PMS were categorized under the name of ***late luteal phase dysphoric disorder*** or LLPDD in the DSM-III-R.
- Renamed ***premenstrual dysphoric disorder*** or PMDD in the appendix of DSM-IV.

PMDD vs. PMS

- PMDD is considered a severe form of PMS.
- Approximately 75% of women have mild to moderate symptoms before their periods which could be considered PMS, requiring little or no treatment.
- 3 to 8% of women have severe, disruptive and disabling premenstrual symptoms known as PMDD – a treatable condition!

What Causes PMDD?

- Largely unknown.
- Research has found no difference in progesterone/estrogen levels throughout cycle in women with or without PMDD.
- However, hormones must play some role because PMDD symptoms resolve with surgical or natural menopause.
- Serotonin? – SSRIs helpful treatment.
- Genetics: 93% identical twins, 44% fraternal twins.
- Psychological, social, cultural factors.

(Endicott)

PMDD – Impact on Society

• Age of Onset	14-17 years
• Prevalence in teenagers	5.3-7.8%
• Duration of disease in women aged 14-51 years	37 years
• Cycles affected: 481-22 (two pregnancies & postpartum periods)	459 cycles
• Average days of severe PMS per cycle	6.1 days
• Total days of disorder	2800 days
• Total years of disorder	7.671 years
• Per 2000 census, women aged 14-51 years in USA	75,580,000
• Women who would meet criteria for PMDD (>5%)	>3,779,000

(Adapted from Murray and Lopez 1996 in Halbreich 2004)

Diagnosing PMDD – Different Patterns Exist

- Symptoms begin at ovulation (mid-cycle), worsen as menses approaches, and end shortly after menses begins.
- Symptoms begin the week before menses and end shortly after.
- Symptoms appear briefly at ovulation, disappear, and reappear before menses….etc.
- To meet diagnosis, symptoms must be absent for at least one week following menses.

(Endicott)

Diagnosing PMDD – DSM IV Criteria

- In most cycles during the past year, five (or more) of the following symptoms with at least one of first four. Symptoms must be present for most of luteal phase and remit within a few days of menses:
  - Marked depressed mood, hopelessness, self-depricating thoughts
  - Marked anxiety, tension, feeling “keyed-up” or “on edge”
  - Marked affective lability
  - Persistent and marked anger or irritability or increased interpersonal conflict
  - Decreased interest in usual activities (work, school, friends, hobbies)
  - Subjective sense of difficulty concentrating
  - Lethargy, easy fatigability, or marked lack of energy
  - Marked change in appetite, overeating, or specific food cravings
  - Hypersomnia or insomnia
  - Sense of being overwhelmed or out of control
  - Other physical symptoms: breast tenderness or swelling, headaches, joint or muscle pain, “bloating”, weight gain

(DSM-IV-TR, 2000)

Diagnosing PMDD – DSM IV Criteria

- The disturbance markedly interferes with work, school, usual social activities, or relationships with others.

- The disturbance is not merely an exacerbation of the symptoms of another disorder (MDD, GAD, BPAD etc.) but may be superimposed on any of these disorders.

- The above criteria must be confirmed by prospective daily ratings during at least **two** consecutive symptomatic cycles.

- Diagnostic Code: **Depressive Disorder NOS** (DSM-IV-TR, 2000)

Diagnosing PMDD in the Clinic

- Clinical Interview
- Physical Exam by primary physician to rule-out medical illness.
- No laboratory tests exist to diagnose PMDD. FSH may be helpful to determine menstrual status in peri-menopausal women.
- Symptom check list (recording for 2 cycles recommended.)

Symptom Check Lists

- **Daily Record of Severity of Problems (DRSP)**
  - http://www.pmdd.factsforhealth.org/have/dailyrecord.html (Jean Endicott, PhD)
  - Good for assessing PMDD.

- **Penn Daily Symptom Rating (DSR)**
  - Ellen W. Freeman, Robert J. DeRubeis and Karl Rickels **Reliability and validity of a daily diary for premenstrual syndrome** *Psychiatry Research, Volume 65, Issue 2, 15 November 1996, Pages 97-106*
  - From Abstract: "Daily ratings of symptoms are essential to confirm a diagnosis of premenstrual syndrome (PMS). The 17-item Daily Symptom Report (DSR) is relatively brief and appropriate for clinical and primary care settings."

- **Calendar of Premenstrual Experiences (COPE)**
  - Mortola JF, Girton L, Beck L, Yen SS. **Diagnosis of premenstrual syndrome by a simple, prospective, and reliable instrument: the calendar of premenstrual experiences.** *Obstet Gynecol*. 1990 Aug;76(2):302-7.

- **Premenstrual Symptom Diary (PMSD)**
  - Dickerson, et al. **Premenstrual Syndrome**. *American Family Physician*. Vol 67. Num 8. April 15, 2003.
  - http://www.aafp.org/afp/20030415/1743.html

Differential Diagnosis –

Mental Disorders That May Have Premenstural Exacerbations

- Major depressive episodes
- Dysthymia
- Chronic major depression
- Bipolar disorder
- Generalized anxiety disorder
- Somatoform disorders
- Personality disorders
- Substance abuse
- Repeated stress
- Attention deficit/hyperactivity disorder

(Halbreich, 2004)

Differential Diagnosis –

General Medical Conditions with Menstrual Exacerbations

- Dysmenorrhea
- Endometriosis
- Polycystic ovaries
- Adverse effects of hormonal contraceptives
- Peri-menopausal symptoms
- Seizure disorder
- Autoimmune diseases (Multiple Sclerosis, Systemic Lupus Erythematosus)
- Hypothyroidism
- Hyperglycemia
- Anemia
- Allergies

(Halbreich, 2004)

Differential Diagnosis –

Disorders with Menstrually-Triggered Episodes

- Epilepsy
- Migraine headache
- Other headaches
- Meningioma symptoms
- Kline-Levin syndrome (hypersomnia)
- Myoclonus
- Neuralgia paresthetica
- Paraparesis
- Autoimmune disease (MS, SLE)
- Suicidal behavior
- Sleep disorders
- Genital herpes
- Asthma
- Pneumothorax
- Pulmonary endometriosis
- Rheumatoid arthritis
- Diabetes mellitus
- Porphyria
- Platelet disorders
- Cholelithiasis
- Urticaria and anaphylaxis
- Glaucoma
- Pain

(Isaacson & Balasubramanyam 1993 in Halbreich 2004)

PMDD – Treatment

Overview

- Many treatments have been used over time for PMS and now PMDD. Only recently have some of these treatments been evaluated in carefully designed studies.

- The list of treatments for PMDD is drawn from:
  - Best available research data
  - Opinions and experience of clinicians
  - Case reports
  - Common sense

PMDD – Treatment

Overview

- Psychotherapy / Behavioral Modification
- Nutritional Remedies
- Herbal Remedies
- Medications
- Other Integrative Remedies
- Surgery

PMDD – Treatment

Psychotherapy / Behavioral Modification

- If possible, start with education, support, and encouragement of lifestyle changes.
- Symptom check list for 2 to 3 months.
- Cognitive Therapy
  - Has been shown to be a promising treatment for PMS. (Morse et al, 1991, in Pearlstein and Steiner)
- Stress Reduction / Relaxation Techniques

PMDD – Treatment

Psychotherapy / Behavioral Modification

- **Exercise**
- **Yoga** – Reduces stress and increases flexability.
- **Meditation**
  - Dharma Singh Khalsa, MD (2001) **Meditation As Medicine**, Fireside, New York.
- **Energy Anatomy** (Mind-Body Connection)
  - Carolyn Myss. (1996) **The Anatomy of the Spirit,** Harmony Books, New York.
  - "The [sexual organs are] your center of personal power, creativity, sexuality, and finances. Issues of physical survival, control, and one-on-one relationships are at the core of this energy center." (www.myss.com)
  - Issues related to sexual organs: Fear of loss of control, or being controlled, through events such as addiction, rape, betrayal, impotence, financial loss, or abandonment by partners or colleagues, ability to take risks, personal identity, blame, guilt, money, sex, power, control, creativity, ethics, honor in relationships, decision-making ability, power to rebel. (www.myss.com)
  - Also see, www.myss.com

PMDD – Treatment

Nutritional Remedies

- **Diet**
  - Eliminate or reduce caffeine, alcohol, chocolate, and tobacco.
  - Adopt a diet with increased protein and limited refined sugar.
  - Decrease sodium in diet when edema or fluid retention occurs.
  - If possible, reduce weight to within 20% of ideal weight.

(Steiner & Born, 2002, in Korstein & Clayton)

PMDD – Treatment

Nutritional Remedies

- **Calcium**
  - Daily supplementation of calcium carbonate containing 1200 mg of elemental calcium has shown to reduce overall luteal phase symptoms
  - 48% reduction with calcium vs. 30% with placebo
  - Symptom reduction occurs by the **third** cycle after starting calcium. (Thys-Jacob & Alvir, 1995, in Chavez & Spitzer) However, some reports that fatigue and insomnia persist.
  - Newer evidence shows that **calcium citrate** may be far better absorbed than calcium carbonate.
  - High Calcium Foods: brocolli, kale, turnip greens, mustard greens, collards, tahini, soy, some tofu, oats, seaweeds, sardines, dairy (yogurt is best source), dried fruit, calcium-fortified juices.
  - Calcium-Rich Herbs: nettles, sage, chickweed, red clover, comfrey leaf, raspberry leaf, oatstraw. (Prepared as tea infusion – 1 pinch herb in hot water = 250 to 300 mg calcium)
  - Avoid alcohol or caffeinated beverages which cause loss of calcium via urine.

(Rosenthal, 2003)

PMDD – Treatment

Nutritional Remedies

- **Magnesium**
  - Evidence exists to suggest that 200 mg of magnesium for a minimum of 2 months may provide benefit for symptoms of fluid retention (weight gain, swelling of extremities, breast tenderness, abdominal bloating.)
  - Food sources: leafy greens, seaweeds, nuts, whole grains, yogurt, cheese, potatoes, corn, peas, squash.
  - Magnesium-Rich Herbs: oatstraw, licorice, kelp, nettles, dulse, burdock, chickweed, althea root, horsetail, sage, raspberry leaf, red clover, valerian, yellow dock, carrot tops, parsley, evening primrose.

- **Vitamin B6**
  - Limited research-based evidence of benefit.
  - "Low-quality" study showing 100 mg daily significantly better than placebo. (Wyatt et al., 1999, in Chavez & Spitzer)
  - High doses of Vitamin B6 are not advised due to risk of nerve damage in some people.

(Rosenthal, 2003)

PMDD – Treatment

Herbal Remedies

- ***Chaste Berry*** (inhibits prolactin release)
  - Commonly used in Europe for PMS symptoms, especially breast discomfort.
  - Multicenter, randomized, double-blind study comparing Chaste Berry to Vit B6 showed both significantly reduce PMS symptoms. (Chaste Berry > Vit B6). No control group in study.
  - Side Effects: nausea, headache, rash. (Lavritzen et al., 1997, in Chavez & Spitzer)

- ***Evening Primrose Oil*** (contains essential fatty acids)
  - European studies suggest improvement in PMS-associated irritability, depression, breast pain and tenderness, headache, and ankle swelling.
  - A review of 5 placebo-controlled studies revealed serious flaws in methodology. Two best studies failed to show improvement. (Horrobin, 1983, in Chavez & Spitzer)

PMDD – Treatment

Medications

- **SSRIs** (Prozac [Sarafem], Paxil CR, and Zoloft are FDA-approved)
  - First-line drugs for premenstrual mood symptoms
  - Also benefit physical symptoms, in particular breast tenderness and bloating.
  - Intermittent administration (luteal phase only) at low-doses (e.g. Prozac 20mg, Zoloft 50mg) has been effective.
  - Response to treatment tends to occur in first month.

(Steiner & Born, 2002, in Korstein & Clayton)

PMDD – Treatment

Medications

- **Anxiolytics**
  - Studies have shown *alprazolam* (*Xanax*, .25 mg tid) and *buspirone* (*Buspar*, 5-10 mg bid or tid) to reduce symptoms, however, the effect was much smaller than that achieved with SSRIs.
  - Intermittent dosing was also effective.
  - Withdrawal, dependence, and tolerance are concerns with *alprazolam (Xanax)* and other benzodiazepines.
  - *Clonazepam* and *lorazepam* may also be helpful.

(Steiner & Born, 2002, in Korstein & Clayton)

- **Diuretics**
  - May decrease water retention, “bloating”, breast tenderness.
  - *Spironolactone* – 50 to 100 mg/day for 5 to 7 days during luteal phase. May have side effects: headache, lethargy, irreg. menses, increased potassium.

- **Pain Relievers**
  - Over the counter (e.g. ibuprofen or naproxen) or prescription.

PMDD – Treatment

Medications

- **Hormones**
  - Chemical Menopause
    - *Leuprolide (Lupron)* – reserved for severe PMDD. Prevents ovulation and may cause premature menopause. May require supplemental estrogen and progesterone.
  - Danazol
    - Synthetic androgen, inhibits LH and FSH secretion, inhibiting estrogen release. Limited use due to multiple side effects.
  - Oral Contraceptives
    - Neither the addition of progesterone or estrogen have scientifically been proven to be beneficial in relieving symptoms despite wide prescription and use. (Endicott)
    - *Yasmin* – new OCP containing estradiol/drospirenone. Possible benefit for physical symptoms
    - High-dose estrogen may be effective, however increases risk of endometrial cancer if not balanced with added progesterone; also, may increase breast cancer risk.
    - Certain types of progesterone may make symptoms worse.
    - *RU-486* given shortly after ovulation blocks progesterone and was found to be 60% effective. Further study needed. (Halbreich)

PMDD – Treatment

Other Integrative Remedies

- Light Therapy
  - Current treatment for Seasonal Affective Disorder.
  - Study of 14 women found benefit with use of 10,000 lux light for 30 minutes in the evening for the 2 weeks before menses onset.
  - Remains experimental. (Endicott)
- Acupuncture or Acupressure

PMDD – Treatment

Surgery

- Surgery is considered a “last resort” treatment for severe, treatment-resistant PMDD.
- Involves removal of both ovaries, therefore inducing a postmenopausal state.
- This postmenopausal state may lead to new problems and health concerns – cardiovascular disease, osteoporosis, hormone replacement therapy.
- Additionally, surgery is not without risks.

PMDD – FUTURE GOALS

- Continued demystification of the menstrual cycle, PMS and PMDD through education of general population and health professionals.

- Continue to clarify and improve recognition, diagnosis, and treatment of PMDD.

- Continued development and scientific evaluation of treatments and remedies for PMDD.

References

- Chavez ML, Spitzer, MF (2002) Herbals and Other Dietary Supplements for Premenstrual Syndrome and Menopause. *Psychiatric Annals*. 32:1:61-71.
- Diagnostic and Statistics Manual of Mental Disorders, Fourth Edition, Text Revision (2000) American Psychiatric Association. pp. 771-773.
- Endicott J, http://www.pmdd.factsforhealth.org.
- Halbreich (2004) The Diagnosis of Premenstrual Syndromes and Premenstrual Dysphoric Disorder – Clinical Procedures and Research Perspectives. *Gynecology Endocrinology*. 19:320-334.
- Kornstein SG, Clayton AH (2002) Women's Mental Health: A Comprehensive Textbook. The Guilford Press. New York.
- Pearlstein T, Steiner M (2000) Non-Antidepressant Treatment of Premenstrual Syndrome. *J Clin Psychiatry*. 61 (suppl 12):22-27.
- Rosenthal MS (2003) The Gynecological Sourcebook, Contemporary Books, The McGraw-Hill Companies.
- Weil VP, Cirigliano MD, Battistini M (2000) Herbal Treatments for Menopause. *Hospital Physician*. pp. 35-44.