Estrogens and Reproductive Depression

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“most common in women of the servant class”
Depression associated with increased incidence of

CHD
Strokes
Hypertension
Metabolic syndrome
Osteoporosis
Alzheimer’s
Non suicide deaths
Obesity

Schmidt P 2007 Menopause international
“Reproductive Depression”


Premenstrual depression

Postnatal depression

Climacteric depression
“Reproductive Depression”


Premenstrual depression
(good mood during pregnancy)

Post natal depression
(return of PMS as periods recur)

Climacteric depression
REPRODUCTIVE DEPRESSION and RESPONSE TO ESTROGENS

Pre-menstrual depression
Magos Studd (1987) BMJ

Post-natal depression

Climacteric depression
Soares 2004 Review

Review Studd J Panay N 2004 Climacteric
EDITORIAL

Why are estrogens rarely used for the treatment of depression in women?

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The short answer to this question could be that they do not work, but that is not true. It is much more likely that a turf war is developing between psychiatrists and gynaecologists/endocrinologists for this common disorder. This is not surprising as we are all products of our training, with hormones and vaginal bleeding an unchartered country for some. As depressed women would normally gravitate to their family doctor and to psychiatrists, it is usual that psychiatric intervention including anti-depressants would be the first line of therapy. However, there are last well, the frequent reply is that it was last pregnancy, several years previously. Postnatal depression occurred, followed by menstrual depression which then became constant as the menopause approached. Patients respond well to moderately high transdermal estrogens. Unfortunately, the history of depression with these reproductive events is sought in a history taking by psychiatrists; the enquiry about how many good days a woman experiences, reveals not only the number of bad days.
Premenstrual Syndrome
or
Premenstrual Dysphoric Disorder
or
misdiagnosed as
Bipolar Disorder
Treatment of PMS (PMDD)
Treatment of PMS (PMDD)

Keep
Treatment of PMS (PMDD)

Keep

Them
Treatment of PMS (PMDD)

Keep Them Away
Treatment of PMS (PMDD)

Keep

Them

Away

From
Treatment of PMS (PMDD)

Keep Them Away From Psychiatrists
Effect of hormones on mood in normal women

- Estrogen very often improves mood
- Testosterone usually improves mood, energy and libido
- Progesterone often produces depression, tiredness, bloating
Hormone therapy for Depression Treatment

• Correct diagnosis
Hormone therapy for depression
Diagnosis of hormone responsive depression

• **Hormone levels not helpful**

• History most important
  1. Relationship to periods
  2. PMS as teenager
  3. History of good mood during pregnancy
  4. History of post natal depression
  5. Often have cyclical menstrual headaches
  6. How many good days a month?
  7. Often becomes worse in the menopausal transition and often improves in the post-menopause
PMS is caused by the cyclical hormonal changes produced by the ovary following ovulation (or anovulatory cycles).

The effective treatment of severe PMS should be based on the abolition of these changes by suppression of ovulation or cyclical ovarian activity.
Hormone therapy for depression

Treatment

• Transdermal E2 100 μg or 200μg patches
• Or gels **Oestrogel or Sandrena**
• Oestradiol implants 50mg for long term therapy
• Often requires plasma levels of >600p.mols for effect and to suppress cycles
• GnRh + “add-back”
Hormone therapy for depression

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- Often requires plasma levels of >600p.mols for effect and to suppress cycles
- GnRh + “add-back”
- Consider adding testosterone for depression and libido
- Require cyclical progestogen or Mirena IUS if patient still has uterus
- Consider TAHBSO + E+T after medical treatment
TAHBSO + HRT

- 14 women
- Unresponsive to conservative therapy
- Danazol completely relieved symptoms
- TAH/BSO effected lasting relief

* Casson I Reid R L; Am J Obstet Gynecol, 1990
TAH BSO for severe PMS (PMDD)

- 47 women over 10 years
- Median age: 42 years (39.8 - 46.6)
- Suffered mean 9.68 years
- Mean treatment prior to referral: 3.57 years
- Mean specialist treatment: 1.21 years

Cronje Vashisht Studd 2004 Human Reprod
Transdermal estradiol and testosterone “always” necessary after TAH+BSO in premenopausal women
Bipolar Disorder or PMS/PMDD?

Longstanding “bipolar depression” diagnosed by psychiatrists often /sometimes disappears when severe PMS / PMDD is treated with transdermal estradiol or TAHBSO
Case History 1

1. First seen Dec 2005 Age 36
2. Many inpatient visits for “manic depression”
3. PMS since teenager
4. Para 2 aged 4 and 3
5. Good mood during pregnancy x2 ➔ PND x2
6. Many SSRIs did not help - did not take suggested Lithium
7. Estradiol patch “99% better” – like pregnancy -- gels implant
8. Progesterone intolerance TAHBSO Oct 07
9. Well no depression no antidepressants.
   Now divorced - much happier

Doctors do not understand what a near death experience cycles can produce
Case History 3

- First met 1968 aged 26
- Depression from aged 20
- Was sterilized age 30 during PhD studies - No children
- Very successful author and academic.
- E and T for PMS/Depression aged 32
- Now aged 67. Well and after 30 years will not come off HRT as her GP suggests
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- Diagnosed Bipolar in USA aged 20.
- Lithium for two years and anti depressants for 20 years
- Sterilized due to misdiagnosis!!
The 8 characteristics of severe PMS not found in bipolar disorder

1. Depression related to menstrual cycle
2. The relief of depression during pregnancy
3. Post natal depression
4. PMDD when periods return
5. PMDD becomes worse with age to perimenopausal depression
6. Co-existence of somatic cyclical symptoms i.e. mastalgia headaches or bloating
7. Usually have monthly runs of 7-10 good days a month
8. Cyclical depression but rarely has highs
PMDD or Bipolar Disorder

1) There was a history of mild or severe PMS as a teenager.

All 10 patients had such a history involving cyclical depression starting soon after puberty. In 5 cases, this was recognized as being a result of simple teenage behavioural and period problems that were not regarded as abnormal, but 4 cases were given antidepressants before the age of 20.
PMDD or Bipolar Disorder

• 2) There was a relief of depressive symptoms during pregnancy

• In all eight of the patents who became pregnant depression was not a problem in 6 who claimed to be in good mood during pregnancy in spite of first trimester problems such as nausea and tiredness but 2 remained on their antidepressants throughout. All eight patients reported that they were at their best with least or no depression during their pregnancies
PMDD or Bipolar Disorder

3 Depression started or recurred post partum as postnatal depression.

• Postnatal depression was a feature in all eight women who had been pregnant but not in every pregnancy. All had antidepressants for postnatal depression and six patients started at this time.
PMDD or Bipolar Disorder

4) Premenstrual depression recurred when menstruation and cycles returned after delivery. All eight women with a pregnancy developed cyclical depression when periods returned with the depression often being more severe than formerly. It was this cyclical depression and lack of response to antidepressants, which led to the diagnosis of bipolar disorder.
PMDD or Bipolar Disorder

5) Premenstrual depression becomes worse with age blending into the menopausal transition and becoming less cyclical.

Although this usually the case it the least helpful of all the questions. The depression can be worse in the menopausal transition and improve when the periods stop after the menopause. It is also advisable to make the diagnosis early and avoid twenty years of inappropriate therapy.
6) There is often co-existence of cyclical somatic symptoms such as menstrual migraine, bloating or mastalgia. These women all had cyclical somatic symptoms lasting from 2 to 14 days each month. All had bloating or mastalgia and 6 had premenstrual or menstrual headaches. These cyclical, mostly progestogenic, symptoms are invariable in PMS / PMDD but do not usually occur in bipolar disorder.
PMDD or Bipolar Disorder

7). They usually have runs of 5-20 good days month

- Although these women may or may not have heavy and painful periods as well as one or two weeks of depression anxiety loss of energy and libido etc all 10 patients had runs of between 5-15 good days a month.

- No patients had episodes of mania.
PMDD or Bipolar Disorder

8) These patients have recurrent episodes of depression, often severe, related to periods but rarely have episodes of mania.

• Nine patients had had no episodes of mania but one had occasionally one or two manic days before a period but none following treatment.

•
Reproductive Depression

In later life after years of depression and antidepressants they will state that they were last well without depression during her last pregnancy.
Safety of estrogens for depression

- Young premenopausal women
- 2002 WHI now mostly discredited
- 2003 MWS never credible except by Oxford epidemiologists
- Transdermal route has little/no effect on hepatic coagulation factors
- Minimal progestogen or none if after hysterectomy
- Latest longitudinal studies of the appropriate age group reveal fewer heart attacks, fewer cardiac deaths and even less breast cancer
- Safer and more effective than antidepressants
Complications of antidepressants and mood stabilizing drugs

- Stroke
- CHD
- Renal failure
- Pregnancy and newborn problems
- Weight gain
- Loss of libido
- Failure of orgasm or erection
- Confusion / sedation
- Tremor
- Overdose / suicide
- Arrhythmias
Complications of antidepressants and mood stabilizing drugs

And they often don’t work!
Transdermal oestrogens in the treatment of postnatal depression
Proportions of subjects scoring above screening threshold for major depression

- **Transdermal oestrogen**
- **Placebo**

% subjects scoring 14+ on EPDS

Time (months) after starting treatment

Baseline | 1 | 3 | 5
“Reproductive Depression”


Premenstrual depression
(good mood during pregnancy)

Post natal depression
(return of PMS as periods recur)

Climacteric depression
Email audit of 238 depressed women treated with estrogens
Studd in press 2014
Email questionnaire of 236 depressed patients

Past medical history

17% had had a “psychotic episode” in the past
58% had seen a psychiatrist
71% had antidepressants prescribed
17% had mood stabilizing drugs
12%(28) had been an in patient for depression
3.8% (9) had received ECT
14% (34) had attempted suicide
Email questionnaire of 236 depressed patients

Association of PMS and PND

162 of 238 (68%) had pms as teenager

145 of 165 (89%) patients who had been pregnant were in good mood without depression during pregnancy but 110 (66%) had postnatal depression

97 (58%) of those pregnant suffered both premenstrual and postnatal depression and 90 (92%) of these were well during pregnancy.
Email questionnaire of 236 depressed patients

**Therapy**

All 238 patients had transdermal estrogens

132 by gel

47 by implant (but always gels first)

59 by both gel and implant

224 (93%) patients also had transdermal Testosterone by gel or implant
Email questionnaire of 236 depressed patients

Progestogen intolerance

63% of the 171 patients who took cyclical progestogen had severe PMS symptoms

59 patients had a Mirena IUS inserted

40 (17%) had a hysterectomy - usually a laparoscopic TAHBSO
Email questionnaire of 236 depressed patients

- 40 women had laparoscopic TAHBSO
- 38 “life changing for the better” - 2 no reply
- 24 no longer on antidepressants
- 6 antidepressants but lower dose
- 10 never had antidepressants
Email questionnaire of 236 depressed patients

How did hormone therapy compare with anti-depressants?

- 37% Did not have anti-depressants
- 61.2% Better
- 6.2% The same
- 0.4% Worse
Email questionnaire of depressed patients

Was hormone therapy life changing for you?

Yes for the better  225(94.2%)

No  13(5.8%)

Yes for worse  0
HRT for

50 year old woman with hot flushes and sweats, vaginal dryness, dyspareunia, loss of libido, depression and low bone density
50 year old woman with hot flushes and sweats, vaginal dryness, dyspareunia, loss of libido, depression and low bone density
PROFOX – A nightmare drug for the future
PROFOX
For more information

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