Sertraline was more effective than desipramine or placebo for premenstrual syndrome

**Freeman EW, Richels K, Sondheimer SJ et al. Differential response to antidepressants in women with premenstrual syndrome/premenstrual dysphoric disorder. A randomized controlled trial. Arch Gen Psychiatry 1999 Oct;56:932–9.**

**QUESTION:** Do women with premenstrual syndrome (PMS) respond differentially to serotonergic antidepressants (ie, sertraline) and noradrenergic antidepressants (ie, desipramine)?

**Design**
3 month randomised (allocation concealed†), blinded [patients, clinicians, outcome assessors, statisticians]‡, placebo controlled trial.

**Setting**
A university hospital in Philadelphia, Pennsylvania, USA.

**Patients**
189 women were enrolled, and 167 (88%) were included in the analysis (mean age 34 y). Women were 18–45 years of age; had regular menstrual cycles of 22–35 days, evidence of ovulation, distressing premenstrual symptoms for ≥6 months, and moderate to severe impairments in work, family life, or social activity; met the criteria for PMS on the Penn Daily Symptom Report (DSR); and had no major psychiatric diagnosis in the previous year. Exclusion criteria included major Axis I syndromes. A total of 36 women were carried forward for 3 months.

**Intervention**
Women were allocated to sertraline, 50–150 mg/day (n = 62, mean dose 105 mg/day); desipramine, 50–150 mg/day (n = 50, mean dose 115 mg/day); or placebo (n = 55) given once each evening for 3 months.

**Main outcome measures**
Premenstrual DSR scores and Hamilton Depression Rating Scale (25 item [HAM-D 25] and 17 item [HAM-D 17] versions) scores for premenstrual days. Secondary outcome measures included the Clinical Global Impressions (CGI) Scale Severity subscale, and self reported Global Ratings of Functioning and Improvement (GRFI).

**Main results**
More women in the sertraline group than the desipramine or placebo groups had a ≥50% decrease in premenstrual symptoms (p < 0.001) and ratings of much or very much improved on the GRFI (p = 0.005) (table). Sertraline led to more women with none to mild symptoms on the CGI Severity scale (p = 0.01) (table) and to lower scores on the HAM-D 17 than did placebo [mean score difference 3.5, 95% CI 1.1 to 6.0].‡

**Conclusion**
Sertraline was more effective than desipramine or placebo for controlling overall premenstrual symptoms and depressive symptoms in women with premenstrual syndrome.

*See glossary.
†Information supplied by author.
‡Calculated from data in article.

**COMMENTARY**

Women in this study by Freeman et al were screened for 3 cycles before inclusion in the treatment phase. This screening included daily DSR ratings for all 3 cycles, HAM-D 25 ratings on days 6–12 for a postmenstrual baseline, a HAM-D 25 premenstrual rating, and a daily single blind placebo during the third cycle. The screening process ensured that inclusion criteria were met. It is interesting to note that more dropouts occurred in the desipramine group than in other groups. Dropouts also tended to have lower DSR scores during the screening periods, which might indicate less severe illness. Furthermore, 74% of the study sample met DSM-IV criteria for premenstrual dysphoric disorder, which means that these women have more severe symptoms that interfere with their functioning. It also is important that anyone taking psychotropic medications or drugs for PMS was excluded.

The results show that sertraline was substantially more effective than desipramine or placebo in reducing symptoms of PMS. Improvement was consistent over all of the rating scales used to monitor symptoms and function. Not to be overlooked is the statement, “Improvement with sertraline treatment occurred swiftly in the first month of double-blind treatment and was maintained in subsequent months.” This is important because it means women can expect some relief from the first cycle they are treated.

Each monthly cycle can be viewed as a “mini-delivery,” much like the withdrawal of oestrogen upon delivery of the placenta at childbirth. According to Genazzani and Bernardi,1 oestrogen promotes the density of serotonin (5-HT2A) binding sites in areas of the brain that influence mood. This may help explain the efficacy of serotonin uptake blockers in treating these illnesses in which symptoms are modulated by changing levels of sex steroids, particularly oestrogen.

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