Oral-Contraceptive Pills to Treat Premenstrual Worsening of Depression

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BACKGROUND

- Depression breaks through premenstrually despite effective depression treatment
- No empiric therapeutic studies
- Do oral-contraceptive pills (OCP) treat PMS?
  - Suggested by ethinyl estradiol and drospirenone (DRSP/EE, Yasmin®) study
  - What is efficacy of OCP in setting of concurrent antidepressant use?

Hypothesis: Stabilization of estradiol and progesterone levels with the OCP Yasmin will treat premenstrual worsening of depression.

METHODS

Subjects
- 18–45-year-old women with regular 25–35-day menstrual cycles
- Depressive disorder in remission 2 months
- 3 months antidepressant use

One-month prospective tracking of PMS to confirm diagnosis
- Daily Record of Severity of Problems Scale (DRSP) increase by 50% from follicular to luteal phase of menstrual cycle
- Montgomery-Åsberg Depression Rating Scale (MADRS) follicular <10, luteal >14

Design
- 2-month treatment with open-label DRSP/EE days 1–21
- Randomized to additional double-blinded EE days 22–28 or placebo with OCP
- Complete daily DRSP and follicular- and luteal-phase MADRS for 2 months

RESULTS

- Of 34 eligible, 17 completed, 6 active (Fig. 1)

- Improvement in MADRS scores (p=0.008, Fig. 3):
  - Premenstrual scores declined (median 20, interquartile range [IQR] 17–23 to median 4, IQR 3–7)
  - Improvement in DRSP scores (p=0.0004, Fig. 4):
  - Premenstrual scores declined (median 58, IQR 45.6–80.8, to median 35.3, IQR 28.4–56)

- DRSP/EE well tolerated (Fig. 1)
- No difference between OCP + day 22 EE vs. OCP + day 22–28 placebo
- Additional observations:
  - DRSP/EE + day 22–28 EE improves premenstrual breakthrough of depression
  - Elimination of hormonal fluctuation and/or suppression of ovulation treats PMS symptoms in women with treated depression
  - Additional stabilization with EE does not appear to confer additional therapeutic advantage
  - OC dysphoria rare
  - Self-reported PMS in women with treated depression prospectively confirmed in most subjects

CONCLUSION

- Self-reported PMS in women with treated depression prospectively confirmed in most subjects

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