

An open-label trial of escitalopram for PPD: Considerations for research

Challenges in recruiting women to postpartum depression (PPD) antidepressant treatment trials, which we encountered when conducting a trial of escitalopram, contribute to the limited body of knowledge about PPD treatment. Here we discuss results from a preliminary trial of escitalopram for PPD, and challenges of research in this area.

Escitalopram, the S-enantiomer of citalopram, is a selective serotonin reuptake inhibitor with high selectivity and potency that is FDA-approved for treating major depressive disorder (MDD) and generalized anxiety disorder. An agent with antidepressant and anxiolytic effects is particularly desirable for PPD because anxiety is more common in postpartum major depressive episodes than non-postpartum MDD.^a Anxiety and depressive disorders commonly are comorbid in postpartum women.^b

We conducted an open-label trial of escitalopram for women with PPD and anxiety. We initially attempted to recruit 20 women.

Methods

Patients received 8 weeks of treatment with escitalopram, 10 to 20 mg/d (flexible dose). After completing the initial phone screen, patients had 5 follow-up visits, once every 2 weeks for 8 weeks. The institutional review board at Massachusetts General Hospital approved this study and we obtained written informed consent from all patients at the first visit. Twelve patients completed the phone screen and 7 eligible patients were enrolled in the study over 32 months. Reasons for ineligibility included having a history of psychosis, onset of symptoms >3 months postpartum, or presenting >6 months after onset. Others declined to participate because of concern about the time commitment or because they pursued nonpharmacologic treatments after the evaluation visit. One patient was lost to follow-up. Three patients completed the study. The study was halted because of the slow pace of recruitment.



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Marlene P. Freeman, MD

Associate Professor of Psychiatry
Harvard Medical School
Director of Clinical Services
Perinatal and Reproductive Psychiatry Program
Massachusetts General Hospital

Hadine Joffe, MD, MSc

Associate Professor
Harvard Medical School
Director of Research
Center for Women's Mental Health
Massachusetts General Hospital

Lee S. Cohen, MD

Carpenter Chair in Psychiatry and Women's Mental Health
Harvard Medical School
Director
Center for Women's Mental Health
Massachusetts General Hospital

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Boston, MA

continued



Postpartum depression

Clinical Point

Two of 3 patients responded to escitalopram ($\geq 50\%$ decrease on MADRS) and both remitted (MADRS score < 7)

Table

Symptom rating scale scores at baseline and study end

| Patient | Baseline (Visit 1) | | | Final (Visit 5) | | |
|---------|--------------------|-----|------|-----------------|-----|------|
| | MADRS | BAI | EPDS | MADRS | BAI | EPDS |
| Ms. A | 21 | 18 | 22 | 12 | 0 | 0 |
| Ms. B | 28 | 28 | 19 | 4 | 5 | 2 |
| Ms. C | 37 | 6 | 19 | 6 | 2 | 0 |

BAI: Beck Anxiety Inventory; EPDS: Edinburgh Postnatal Depression Scale; MADRS: Montgomery-Åsberg Depression Rating Scale

Patient selection. Patients were screened for a major depressive episode with postpartum onset within 3 months of childbirth; depressive symptoms may have developed during pregnancy and worsened postpartum to meet criteria for MDD. Women were eligible for the study if they:

- were age 18 to 45
- experienced a major depressive episode with symptoms developing within 3 months of childbirth
- presented within 6 months of childbirth
- had a Montgomery-Åsberg Depression Rating Scale (MADRS) score ≥ 15
- had a Beck Anxiety Inventory (BAI) score ≥ 10 .

Patients who were pregnant or breastfeeding were excluded from the study per an agreement with the sponsor. In addition, women were excluded if they had taken any psychotropic medication within 2 weeks of enrollment; had active suicidal ideation, homicidal ideation, or presence of psychotic symptoms; had chronic depression or dysthymia; had chronic or treatment-resistant anxiety disorders; had a history of mania or hypomania; or had active alcohol or substance abuse within the past year.

Treatment. Patients received escitalopram, 10 mg/d, after the baseline visit. At the investigator's discretion, the dose could be increased to 20 mg/d or lowered to 5 mg/d if side effects occurred.

Measures. At the first visit, patients were assessed with the Mini-International Neuropsychiatric Interview to verify MDD and exclude diagnoses that would determine ineligibility. MADRS and Edinburgh Postnatal Depression Scale (EPDS) were

used at each visit to measure depressive symptoms.^{c,d} The BAI was completed at each visit to measure anxiety symptoms. Obsessions and compulsions were measured with the Yale-Brown Obsessive Compulsive Scale (Y-BOCS)^e at baseline, and at all following visits if the patient scored > 8 at baseline. The Clinical Global Impression Scales for severity and improvement were completed at each visit.^f

Results

Of 7 patients enrolled, 3 completed the study, 2 were ineligible after the baseline visit, and 2 did not participate after the baseline visit (1 selected to pursue psychotherapy, and 1 was lost to follow-up).

Two of 3 patients responded to escitalopram ($\geq 50\%$ decrease on MADRS), and both were remitters (MADRS score < 7). All 3 patients were responders on EPDS and BAI. One patient had Y-BOCS > 8 at baseline (Total Y-BOCS score of 9, and final Y-BOCS score of 8) (Table).

Discussion

Patients who stayed in treatment improved during the course of this study. Recruitment was difficult; we were able to recruit only 7 patients out of a projected 20 for the screening visit. We solicited feedback from local obstetrics health care providers and social workers on recruitment and attractiveness of the study as part of our routine collaboration with obstetrical services that screen for PPD. Primary reasons patients were not referred were that they were breastfeeding or they stated they would prefer to receive treatment from their primary care doctor.

Recruitment difficulty in this study was in stark contrast to other recent studies completed at our center. For example, we have successfully recruited for menopausal depression and premenstrual dysphoric disorder treatment studies, and have completed large naturalistic studies of women with unipolar depression and bipolar disorder across pregnancy and postpartum. We suspect that many patients who were eligible for the study preferred to seek care from an obstetrician or primary care doctor with whom they already had a therapeutic alliance, and we also suspect that many women with PPD do not seek treatment at all, which is consistent with findings from other research groups.

Lessons learned from PPD research include:

- Including women who are breast-feeding is important because many women choose to breast-feed and suffer from PPD. Because antidepressant use during breast-feeding has been closely studied, it is appropriate to include potential research participants who are breast-feeding as long as they receive adequate information and are able to provide informed consent.

- Participants in PPD studies may require accommodations that take into account their role as a new mother, such as on-site childcare, home visits, or other strategies.

- Because of recruitment challenges in postpartum patients, multisite trials may be required to include adequate numbers of participants.

Related Resource

- Freeman MP, Joffe H, Cohen LS. Postpartum depression: Help patients find the right treatment. *Current Psychiatry*. 2012;11(11):14-21.

Drug Brand Names

Citalopram • Celexa

Escitalopram • Lexapro

Disclosures

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