

# Evidence in practice – number 7

## Can postpartum depression be prevented?

**Clinical question – is there any preventive treatment for postpartum depression in a lady with previous episodes?**

This question was sent to us at the Centre for General Practice, University of Queensland, Australia. We were providing a literature search service in collaboration with the Department of Primary Health Care at the University of Newcastle upon Tyne (funded through the NHS Northern and Yorkshire Regional Library Advisory Service), for GPs in the North of England, modelled on one run in Australia.<sup>1</sup> GPs sent requests for answers to questions arising during clinical consultations. We then undertook a search for the best available published evidence, briefly interpreted it, and quickly (within days) returned the answer to the GP.

Our response to one of the questions received is presented. Under the Update section, we present relevant research published subsequent to the initial search.

### SEARCH QUESTION

First, the clinical question was reformatted into a 'searchable question':<sup>2</sup>

**In women with previous episodes of postnatal depression, how effective are pharmaceutical and/or non-pharmaceutical interventions for preventing recurrence?**

The ideal study to answer this question would be a randomised trial (or preferably a systematic review of trials) in women with previous episodes of postnatal depression, of pharmaceutical and or non-pharmaceutical treatments compared to a 'control' treatment.

### SEARCH

We searched the Cochrane Library and PubMed using combinations of the following text and MeSH search terms:

'depression postpartum (MeSH and text)' OR 'postnatal depress\*' OR 'postpartum depress\*' OR 'post\*natal depress\*' AND 'prevent\*' OR 'prophyla\*'.  
**SUMMARY OF FINDINGS**

### SUMMARY OF FINDINGS

We located only one non-randomised study evaluating the effectiveness of postpartum monitoring alone compared to monitoring and antidepressant treatment (with either the medication that had been effective for the previous episode or nortriptyline) for the prevention of recurrent episodes of postnatal depression.<sup>3</sup> The study was not of high quality (open label and non-randomised) and the sample size ( $n = 23$ ) small. In this study, a significantly greater proportion of women ( $P < 0.05$ ) who elected monitoring alone (63%) suffered recurrence of major depression compared with the women who received monitoring and medication (7%).<sup>3</sup>

We were unable to locate any trials evaluating hormonal or non-pharmaceutical interventions specifically in women with a previous episode of postpartum depression. We provided a summary of the results of trials of non-pharmaceutical interventions conducted in women without previous episodes, and reported a systematic review of trials evaluating the preventive effect of oestrogens and progestin.<sup>4</sup>

### MANAGEMENT OUTCOMES OF THIS PATIENT

Not known.

### UPDATE

The original search was conducted in January 2001. Repeating the search in March 2005 identified two additional trials of drug treatments in women with a previous episode of postpartum depression. In the first, women with at least one past episode of postpartum major depression were randomised to receive either the tricyclic antidepressant

nortriptyline or placebo in a double blind trial.<sup>5</sup> At 20 weeks post-intervention, there was no difference between the rate of recurrence in women treated with nortriptyline (0.23, 95% confidence interval [CI] = 0.01 to 0.44) and placebo (0.24, 95% CI = 0.01 to 0.45). The second randomised pilot trial of 17 patients evaluated the effect of the selective serotonin reuptake inhibitor sertraline versus placebo.<sup>6</sup> At 17 weeks the rate of recurrence for the sertraline and placebo groups was 7% (95% CI = 0.00 to 0.34) and 50% (95% CI = 0.01 to 0.84), respectively ( $P = 0.04$ ). The time to recurrence was also significantly longer in the sertraline treated women.

### COMMENT

This is a good example of the fact that the best available evidence changes as new research data become available. The contrasting results of the three trials<sup>4-6</sup> conducted in women with previous episodes of postpartum depression may be explained in part by differences in trial methodology and/or the preventive efficacy of different drug classes. The positive result of the earliest trial (of nortriptyline or other antidepressant against placebo) may be an artefact produced because of its inferior methods (non-randomised and non-blind, which allow selection bias; the women feeling themselves to be at greatest risk opting for treatment, for example, and response bias; those using antidepressants perhaps being more greatly influenced by a placebo effect). The more recent trial of nortriptyline is less subject to these biases and found no benefit.

The pilot trial evaluating sertraline, however, reported a positive effect.<sup>6</sup> Differing modes of action of the two classes of drugs may explain the difference in preventive efficacy, but this was a very small trial (only 17 patients), and the very high recurrence rate in the placebo group

(4/8 = 50%) is hard to reconcile with earlier experience.

While adverse events occurred more frequently among women receiving sertraline, again because of the small numbers in the trial, this could be a chance occurrence. And of course, trial data are not the best source of evidence for rare adverse events, for which huge patient numbers are required. There are minimal data on which to base decisions about the safety of breastfeeding while taking sertraline. Expert Consensus Guidelines<sup>7</sup> based on multiple case series by several investigators suggest that sertraline may be used with minimal risk in breastfeeding mothers; however, there are no published controlled long-term evaluations of infants exposed to selective serotonin reuptake inhibitors through breast milk.<sup>8</sup>

The updated search also located two Cochrane reviews<sup>9,10</sup> and a review protocol<sup>11</sup> that seemed relevant, although the trials included in these reviews did not necessarily enrol women with previous episodes of postpartum depression. One of the reviews (including only two trials) found that synthetic progestogen increased the risk of postpartum depression and reported that the preventive effect of oestrogens is unknown.<sup>9</sup> In another review, the effect of psychosocial and psychological interventions for preventing postpartum depression was evaluated.<sup>10</sup> In a subgroup analysis (specified *a priori*), the effect of a variety of non-pharmaceutical interventions was evaluated in women defined as 'high risk' and the general population: trials selecting participants based on 'at risk' criteria had more apparent success in preventing postpartum depression (relative risk [RR] = 0.67, 95% CI = 0.51 to 0.89) than those enrolling women from the general population (RR = 0.87, 95% CI = 0.66 to 1.16). Given that a previous episode of

depression (of any type) is one of the strongest risk factors for a future episode,<sup>12</sup> these data (which should be interpreted cautiously) suggest a possible alternative to antidepressant treatment for this woman. A review evaluating the effectiveness of antidepressant drugs in the prevention of postpartum depression is currently only in protocol form.<sup>11</sup>

**SHARON SANDERS  
CHRIS DEL MAR  
SARAH PURDY  
ANNELISE SPINKS  
LISA TAIT  
BRIAN McAVOY**

#### REFERENCES

1. Del Mar CB, Silagy CA, Glasziou PP, *et al.* Feasibility of an evidence-based literature search service for general practitioners. *Med J Aust* 2001 **175**(3): 134–137.
2. Centre for Evidence-Based Medicine. Focusing clinical questions. [http://www.cebm.net/focus\\_quest.asp](http://www.cebm.net/focus_quest.asp) (accessed 11 Apr 2005).
3. Wisner KL, Wheeler SB. Prevention of recurrent postpartum major depression. *Hosp Community Psychiatry* 1994; **45**(12): 1191–1196.
4. Lawrie TA, Herxheimer A, Dalton K. Oestrogens and progestogens for preventing and treating postnatal depression (Cochrane Review). In: *The Cochrane Library*, Issue 2, 2003. Oxford: Update Software.
5. Wisner KL, Perel JM, Peindl KS, *et al.* Prevention of recurrent postpartum depression: a randomised clinical trial. *J Clin Psychiatry* 2001; **62**(2): 82–86.
6. Wisner KL, Perel JM, Peindl KS, *et al.* Prevention of postpartum depression: a pilot randomised clinical trial. *Am J Psychiatry* 2004; **161**(7): 1290–1292.
7. Altshuler LL, Cohen LS, Moline ML, *et al.* The Expert Consensus Guideline Series: treatment of depression in women. [review.] *Postgrad Med* 2001; (**Spec No**): 1–107.
8. Yoshida K, Smith B, Kumar R. Psychotropic drugs in mothers' milk: a comprehensive review of assay methods, pharmacokinetics, and of safety of breastfeeding. *J Psychopharmacol* 1999; **13**(1): 64–80.
9. Dennis CL, Ross LE, Herxheimer A. Oestrogens and progestins for preventing and treating postpartum depression. [review.] *The Cochrane Database of Systematic Reviews* 1999, Issue 2. Art. No.: CD001690. DOI: 10.1002/14651858.CD001690.
10. Dennis C-L, Creedy D. Psychosocial and psychological interventions for preventing postpartum depression. [review.] *The Cochrane Database of Systematic Reviews* 2004, Issue 4. Art. No.: CD001134. DOI: 10.1002/14651858.CD001134.pub2.
11. Howard LM, Hoffbrand S, Henshaw C, *et al.* Antidepressant prevention of postnatal depression. [protocol.] *The Cochrane Database of Systematic Reviews* 2003, Issue 3. Art. No.: CD004363. DOI: 10.1002/14651858.CD004363.
12. Robertson E, Grace S, Wallington T, Stewart DE. Antenatal risk factors for postpartum depression: a synthesis of recent literature. *Gen Hosp Psychiatry* 2004; **26**: 289–295.