Weight Changes in Postpartum Women With Remitted Depression

Barbara L. Gracious, M.D.; Barbara H. Hanusa, Ph.D.; Katherine L. Wisner, M.D.; Kathleen S. Peindl, Ph.D.; and James M. Perel, Ph.D.

Objective: To compare weight loss after birth in women who took the antidepressants nortriptyline or sertraline or placebo in 2 clinical studies designed to prevent recurrent postpartum major depression.

Method: Data were collected from 1995 to 2001. All subjects had at least 1 prior episode of Research Diagnostic Criteria– or DSM-IV–defined major depressive disorder. Data on weight were available for 467 weeks from 60 women who were weighed 8 times from 2 to 17 weeks postpartum. The dependent measures were weight at weeks 11 and 17 and weight change from weeks 2 to 17 postpartum.

Results: At week 17, the women's weights ranged from 109 to 268 lb. Their weight change ranged from +14 to –19 lb over the 15-week postpartum period (mean = –1.8, SD = 5.1 lb). After controlling for week 2 weights, the mean weights at week 17 for the women treated with nortriptyline, sertraline, or placebo were not significantly different. Of 60 women with 3 or more weight assessments, those who were randomly assigned to nortriptyline lost weight more rapidly than the other 2 groups; however, the mean weight change across all groups was only –1.8 lb (SD = 5.1 lb).

Conclusions: Weight loss was not compromised by antidepressant pharmacotherapy. Postpartum weight retention occurred in this group of nondepressed women with previous histories of major depression independent of drug treatment.

(J Clin Psychiatry 2005;66:291–293)

Received April 28, 2004; accepted Sept. 2, 2004. *From the Departments of Psychiatry and Obstetrics and Gynecology, University of Rochester Medical Center, Rochester, N.Y. (Dr. Gracious); the Department of Medicine (Dr. Hanusa), the Departments of Psychiatry and Obstetrics and Gynecology and Reproductive Sciences and Epidemiology (Dr. Wisner) and the Departments of Psychiatry and Pharmacology, Western Psychiatric Institute and Clinic (Dr. Perel), University of Pittsburgh School of Medicine, Pittsburgh; and the Department of Psychiatry, Thomas Jefferson University, Philadelphia (Dr. Peindl), Pa.*

This study was supported by National Institute of Mental Health grant RO153735: Prevention of Recurrent Episodes of Postpartum Major Depression to Drs. Wisner and Perel, and National Institute of Mental Health Clinical Pharmacology Core grant 30915 to Dr. Perel.

Dr. Wisner has served as a consultant to and received honoraria from Sepracor and has participated in speakers' or advisory boards for Pfizer, GlaxoSmithKline, and Sepracor.

Corresponding author and reprints: Katherine L. Wisner, M.D., Departments of Psychiatry, Obstetrics and Gynecology and Reproductive Sciences and Epidemiology, Women's Behavioral HealthCARE, Western Psychiatric Institute and Clinic, 3811 O'Hara St., Pittsburgh, PA 15213 (e-mail: WisnerKL@upmc.edu).

Postpartum weight is an important predictor of psychological health following birth[1]; however, difficulty returning to pre-pregnancy body weight is a common problem in affluent countries. Surprisingly, there are no established norms for weight loss following pregnancy. In one study of 2295 Swedish women, investigators reported a mean 10-kg (22-lb) weight loss in the first 10 weeks after delivery.[2] Other investigators have found an average of 0.5 to 1.5 kg (1.0–3.3 lb) gained at 6 to 12 months after delivery compared with the pre-pregnancy weight.[3,4] Ohlin and Rossner[2] studied weight change 1 year after delivery and found that 30% of subjects lost weight, 56% gained 0 to < 5 kg, 13% gained 5 to 10 kg, and 1.5% gained more than 10 kg. The percentage of overweight women increased from 13% to 21%.

Factors that affect postpartum weight loss include pre-pregnancy weight, weight gain in the current pregnancy,[2,4] gain following prior pregnancies,[2] age, parity, breast-feeding status, working status,[4,5] smoking cessation,[2] and race.[3,6] Studies of patterns of weight change after delivery in women are critical, since postpartum weight retention is a significant contributor to the current epidemic of obesity in America.[7,8]

Postpartum weight retention is an important factor to consider when assessing maternal health and pregnancy outcomes.[7] In 1990, the Institute of Medicine (IOM)[9] provided target ranges of recommended weight gain for pregnant women that were based on pre-pregnancy body mass index (BMI). For example, for a woman with a normal BMI (19.8–26.0 kg/m^2) at conception, the optimal weight gain is 11.5 to 16.0 kg. Studies reviewed by the IOM suggested an average weight retention in mothers of 1 kg per birth, but weight gains were lower than those currently observed in the United States.[7] Weight gains within the IOM's recommended ranges were associated with better pregnancy outcomes than were weight gains outside the ranges. Weight gains within the IOM-specified ranges did not result in substantive postpartum weight retention.

We evaluated postpartum weight loss in 2 randomized clinical trials[11,12] designed to prevent postpartum major depression. Our hypotheses were that (1) women treated with nortriptyline would weigh more at week 17 postpartum than women assigned to placebo and have a slower rate of weight loss than women assigned to placebo and

(2) women treated with sertraline would lose weight at a rate similar to women treated with placebo. These hypotheses were based on reports that tricyclics such as nortriptyline are more likely to be accompanied by weight gain (and by analogy weight retention postbirth) than are the selective serotonin reuptake inhibitors such as sertraline.[10] To our knowledge, this is the first time a placebo-controlled study has been examined for the effect of antidepressant treatment on weight loss in the postpartum period.

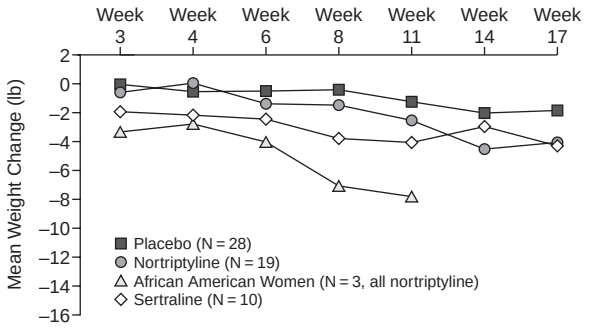
METHOD

We studied women enrolled in 2 double-blind randomized clinical trials (RCTs) designed to test the effectiveness of nortriptyline (N = 25) versus placebo (N = 26)[11] and sertraline (N = 14) versus placebo (N = 8)[12] for the prevention of recurrent postpartum major depression. Women eligible for the trials were pregnant (≤ 35 weeks' gestation), aged 18 to 45 years, and had at least 1 prior episode of Research Diagnostic Criteria– or DSM-IV–defined major depressive disorder. They must have been remitted from depression during the index pregnancy to enter the prevention trial. Medication was begun within 48 hours of delivery. Women were treated for 17 weeks with nortriptyline, sertraline, or placebo, after which medication was tapered and withdrawn by week 20 postpartum. Women were weighed at 2, 3, 4, 6, 8, 11, 14, and 17 weeks postpartum.

Women with other active comorbid Axis I disorders, with the exception of generalized anxiety or panic disorder, were excluded from this investigation. Women with eating disorders were excluded. Written informed consent was obtained from each subject. Data were collected from 1995 to 2001.

At week 17, the weights of women assigned to nortriptyline or sertraline were compared with the weights of women assigned to placebo by using analysis of covariance to control statistically for week 2 weights. The observed standard deviations of weight were unequal across the drug and placebo groups. On examination of the distributions of the weights, it was clear that the 4 women who weighed over 240 lb were skewing the distribution. They were excluded from the analyses that relied on normally distributed data. Changes in weight from weeks 2 to 17 were normally distributed and were analyzed with random effects regression. Women who developed postpartum major depression during the 17-week trial (N = 10) were censored at the time of recurrence to remove the effects of recurrent, active depression upon weight. Weight change was analyzed with and without controlling for variables associated in previous work on postpartum weight changes (history of nonpostpartum major depression, baseline weight, race, marital status, parity, socioeconomic status, and breastfeeding).

Figure 1. Mean Postpartum Weight Change in Women Treated With Nortriptyline, Sertraline, or Placebo



RESULTS

Of the 44 women with weight available at week 17 (range, 109–268 lb), 1 assigned to placebo was > 240 lb at baseline and 17 weeks. In the 43 remaining women, those assigned to nortriptyline (N = 17, mean weight = 160.3 lb, SD = 23.2) were heavier than those assigned to either sertraline (N = 7, mean weight = 144.1 lb, SD = 20.9) or placebo (N = 19, mean weight = 142.5 lb, SD = 18.5) ($F = 3.61$, $df = 2,40$; $p = .04$). At baseline (week 2), women assigned to nortriptyline were heavier (mean weight = 164.4, SD = 23.5) than women assigned to sertraline (mean weight = 148.6 lb, SD = 19.1) or placebo (mean weight = 144.9 lb, SD = 17.7) ($F = 4.34$, $df = 2,40$; $p = .02$). With baseline weight as a covariate, the difference in weight between groups at week 17 was eliminated ($F = 0.28$, $df = 2,39$; $p = .8$).

Weight data for at least 3 assessment times were available for 60 women who produced 467 weeks of measurements. Three women (5.0%) were African American. In these 60 women, baseline weights ranged from 107 to 296 lb (mean weight = 163.0 lb, SD = 37.4). Excluded from the initial modeling of weight and weight change were 5 women (2 African American) who had weights greater than 240 lb. The mean postpartum weight changes for the 60 women in the sample are displayed in Figure 1. Weight change across the 15 weeks ranged from –19 lb to +14 lb (mean = –1.8, SD = 5.1). Because women who suffered recurrence were censored, we also analyzed data at week 11, when weight data were available for 55 women. The mean weight loss at week 11 was only 2.5 lb (SD = 5.9, range, –19 to +11 lb). Ten women consistently gained weight (mean change = +4.5 lb, SD = 3.1), 18 women fluctuated between gain and loss (mean change = –0.28 lb, SD = 4.0), and 27 women consistently lost weight (mean change = –6.5 lb, SD = 4.3). There were no differences in weight loss at week 11 across the active drug or placebo groups.

In regression modeling of weight change, we found that race, heavy weight (greater than 240 lb), history

of nonpostpartum major depressive episodes, and drug status were not independent. Initial modeling of the importance of drug status and prior nonpostpartum major depressive episodes was performed with women who weighed less than 240 lb. Weight change was significantly associated with drug status and prior nonpostpartum depression. Women who took nortriptyline lost more weight (drug-by-weeks coefficient = –0.20, 95% confidence interval (CI) = –0.07 to –0.32), as did women with prior nonpostpartum major depression, than did women with postpartum depression only (major depression-by-weeks coefficient = –0.44, 95% CI = –0.33 to –0.55). With all subjects in the model, race was significantly related to weight change (coefficient for race by week = –0.35, 95% CI = –0.03 to –0.66). African American women, who were heavier at baseline, lost more weight than did white women. Sertraline treatment, baseline weight, breastfeeding status, age, parity, marital status, socioeconomic status, and recurrence of depression were not associated with weight change.

DISCUSSION

These data refute our hypotheses that women treated with nortriptyline in the postpartum period would weigh more at the end of the RCT and have a slower rate of weight loss than women assigned to placebo. Our hypothesis that women treated with sertraline would lose weight at a rate similar to those treated with placebo was confirmed. Concern about compromised weight loss in postpartum women treated with either nortriptyline or sertraline is unwarranted. In fact, the striking finding from this study is the minimal weight loss from weeks 2 to 17 across all groups (sertraline, nortriptyline, and placebo). These data are unique in that (1) antidepressant treatment occurred without the concomitant presence of major depression so that weight effects could be assessed without co-occurring appetite and food intake symptoms related to depressive disorder and (2) a placebo-treated group was included.

The effect of antidepressant treatment upon weight is complicated because appetite and weight change are symptoms of the disorder for which the drugs are used.[10] Weight gain may occur as an indication of recovery in women who had weight loss due to depression. In women with atypical depression features, weight gain is present as part of the depressive syndrome and may be exacerbated by drug treatment. The weight status of depressed and recovered women of childbearing age is affected by drug treatment and disease factors as they enter pregnancies. Since minimal weight loss occurred in our placebo-treated as well as drug-treated groups, nondepressed women with a history of major depression appear to be at risk for weight retention after delivery. Additional questions raised by this report are whether women with histories of major depression (compared with women without such histories) (1) have a higher BMI at conception, (2) gain weight according to the IOM recommended ranges, and (3) have greater weight retention after birth. Our research group is evaluating these questions in a prospective study of 3 groups of women: depressed, antidepressant-treated, and nondepressed, nontreated women during pregnancy and through 2 years postpartum.

Drug names: nortriptyline (Pamelor, Aventyl, and others), sertraline (Zoloft).

REFERENCES

1. Jenkin W, Tiggemann M. Psychological effects of weight retained after pregnancy. Women Health 1997;25:89–98
2. Ohlin A, Rossner S. Maternal body weight development after pregnancy. Int J Obes 1990;14:159–173
3. Boardley DJ, Sargent RG, Coker AL, et al. The relationship between diet, activity, and other factors, and postpartum weight change by race. Obstet Gynecol 1995;86:834–838
4. Schauberger CW, Rooney BL, Brimer LM. Factors that influence weight loss in the puerperium. Obstet Gynecol 1992;79:424–429
5. Keppel KG, Taffel SM. Pregnancy-related weight gain and retention: implications of the 1990 Institute of Medicine Guidelines. Am J Public Health 1993;83:1100–1103
6. Smith DE, Lewis CE, Caveny JL, et al. Longitudinal changes in adiposity associated with pregnancy. JAMA 1994;271:1747–1751
7. Abrams B, Altman SL, Pickett KE. Pregnancy weight gain: still controversial. Am J Clin Nutr 2000;71(suppl 5):1233S–1241S
8. Harris HE, Ellison GTH. Do the changes in energy balance that occur during pregnancy predispose parous women to obesity? Nutr Res Rev 1997;10:57–81
9. Institute of Medicine. Nutrition During Pregnancy, Weight Gain and Nutrient Supplements. Report of the Subcommittee on Nutritional Status and Weight Gain during Pregnancy, Subcommittee on Dietary Intake and Nutrient Supplements during Pregnancy, Committee on Nutritional Status during Pregnancy and Lactation, Food and Nutrition Board. Washington, DC: National Academy Press; 1990:1–233
10. Fava M. Weight gain and antidepressants. J Clin Psychiatry 2000;61 (suppl 11):37–41
11. Wisner KL, Perel JM, Peindl KS, et al. Prevention of recurrent postpartum depression: a randomized clinical trial. J Clin Psychiatry 2001;62:82–86
12. Wisner KL, Perel JM, Peindl KS, et al. Prevention of postpartum depression: a pilot randomized clinical trial. Am J Psychiatry 2004;161: 1290–1292