Menopausal Hormones May Bring on Depression

BY MARY ANN MOON
Contributing Writer

The "changing hormonal milieu" of menopause is strongly associated with new-onset major depression in women with no history of mood disturbance, reported Ellen W. Freeman, Ph.D., of the departments of ob.gyn. and psychiatry at the University of Pennsylvania, Philadelphia, and her associates.

Women are significantly more likely to develop a depressive disorder when their levels of estradiol fluctuate, levels of FSH and LH increase, and levels of inhibin B decrease, as happens during the transition to menopause. It appears that the hormonal changes characteristic of ovarian aging produce "destabilizing effects" that contribute to depression, Dr. Freeman and her associates in the Penn Ovarian Aging Study commented. This finding should make a substantial contribution to what has been only "limited evidence" in the literature about mood symptoms in the perimenopausal years. "Whether mood symptoms increase in the perimenopausal years and whether the occurrence of depressed mood is independently associated with ovarian changes is secondary to vasomotor or other bothersome symptoms" has been controversial, they noted.

Dr. Freeman and her associates examined thee issue by assessing fluctuations in reproductive hormone levels in 231 premenopausal women aged 35-47 years at baseline who were followed for 8 years. During that interval, 43% of the women entered the transition to menopause.

Hormone assays were conducted in 10 assessment periods, the first 6 at 8-month intervals. Blood samples were collected at the start of menstrual cycles, and subjects also were interviewed concerning their overall health, demographic factors, and menopausal symptoms. Depressive symptoms were assessed using the CES-D (Center for Epidemiological Studies-Depression) scale; either the PRIME-MD (Primary Care Evaluation of Mental Disorders) or the PHQ (Patient Health Questionnaire) was used to detect major depressive disorder.

A total of 116 women (50%) was found to have depressive symptoms on the CES-D during follow-up. Of these, 16 women had depressive symptoms on two consecutive assessments and 35 had them on three or more consecutive assessments. Of the 231 women, 59 (26%) were found to have depressive disorders on the PRIME-MD or PHQ; 26 had major depressive disorder and 33 had other depressive disorders. Nine of the women had depressive disorders on two consecutive assessments and four had them on three or more consecutive assessments.

A total of 108 women (47%) showed no depressive symptoms on either measure, the researchers said (Arch. Gen. Psychiatry 2006;63:375-82). Changes in individual women's levels of FSH, LH, and inhibin B were significantly associated with depressive symptoms and with major depression. Similarly, variability in a woman's mean levels of estradiol, FSH, and LH also were linked to depression and depressive symptoms. "On average, the women were 4.58 times more likely to have higher FSH levels ... 3 times more likely to have higher LH levels ...and 63% more likely to have lower inhibin B levels ... at the time of high [depression] scores" compared with the time before high scores, the investigators wrote.

After the data were adjusted for several other depression risk factors, including change in employment status or marital status, the researchers found that a woman was, on average, more than five times "more likely to be in menopausal transition at the time of reporting high [depression] scores than she was before the onset of depressive symptoms." The "strongest risk factor for the new onset of diagnosed depressive disorders was the increased variability of estradiol (around the woman's own mean levels) at the time of the diagnosed disorder," Dr. Freeman and her associates said.

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Dr. Freeman