Depression increases in women during early to late menopause but decreases after menopause

Freeman EW, Sammel MD, Liu L, *et al.* Hormones and menopausal status as predictors of depression in women in transition to menopause. *Arch Gen Psychiatry* 2004;**61**:62–70.

Q Is there an association between depression and the transition to menopause?

METHODS

Design: Longitudinal prospective cohort study.

Follow up period: Four years.

Setting: Philadelphia County, USA; timeframe not stated

People: 436 initially premenopausal women (218 white, 218 African American; mean age at endpoint 44.6 years, range 38–52 years) with 22–35 day menstrual cycles, an intact uterus and at least one ovary. Exclusions: psychotropic or hormonal medication, pregnancy, breastfeeding, compromised ovarian function, or substance abuse.

Risk factors: Data were collected during six assessments, approximately every 8 months. Trained researchers collected blood samples for hormone assays (obtained between days 2 and 6 of consecutive menstrual cycles); administered a structured interview to assess general health status and behaviour, and the Center for Epidemiology Studies Depression Scale (CES-D). Major depressive disorder was assessed according to DSM-IV criteria. At each interview, menopausal status was determined.

Outcomes: Depressive symptoms (CES-D; a cut off score of ≥ 16 defined high depressive symptoms); MDD; menopausal status determined with the Staging System for Reproductive Aging in Women (premenopausal: regular 22–35 day menstrual cycle; early menopause: change in cycle length by more than a week for two cycles; late menopause: absence of menstruation for 3–11 months; postmenopausal: absence of menstruation for more than 12 months); predictor variables (including hot flashes, sleep pattern, employment status, history of depression, PMS severity).

MAIN RESULTS

Data are presented for 76% of the original sample (332 women). 21% of women had a history of depression at baseline. At 4 years, 3% were postmenopausal, 3% in late menopause, 21% in early menopause, and 73% remained premenopausal. Depressive symptoms were more likely during early and late transition to menopause than pre or post menopause. History of depression, severe PMS, and poor sleep increased likelihood of depression in menopausal women (see <http://www.ebmentalhealth.com/supplemental> for table).

CONCLUSIONS

Depression significantly increases in women as they reach menopause but decreases once menopause is complete.

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Commentary

The study by Freeman and colleagues is important because it periodically obtained blood samples from a prospective cohort of premenopausal women not initially using hormones, who were followed over a significant number of years (4 years). Consistent with prior work, depressive symptoms, as measured by the CES-D, significantly increased during the perimenopausal stage and decreased after menopause. However, the question of whether hormonal shifts during perimenopause increased depressive symptoms, or that climacteric symptoms were interpreted as depressive symptoms remains unanswered. It is unclear whether clinicians should treat the depressive symptoms, treat the climacteric symptoms, a combination of the two, or wait until women pass through to menopausal stages.

Randomised placebo controlled trials have not consistently found that use of an oestrogen/progesterone combination improves mood.^{1–3} However, in the HERS trial, the benefit of hormone therapy (HT) was observed among women experiencing flushing,⁴ but no significant relation was observed for women not experiencing flushing. The frequent administration of progesterone with oestrogen confounds exploration of the antidepressant role of HT. In our own study of community women aged 45–54 years, increased climacteric symptoms (hot flashes, trouble sleeping, night sweats, memory problems, mood swings) explain the observed increased rates of depressive symptoms among women of this cohort (almost 30% reported high levels of depressive symptoms as measured by a shortened CES-D).⁵ Even after considering HT, climacteric symptoms remained significantly related to increased depressive symptoms.

Although there is suggestive evidence from observational studies and a limited number of randomised, controlled trials that oestrogen therapy improves mood and cognition, the clinical relevance of oestrogen administration is unproved. There are weak data that oestrogens might be considered for mild depressive symptoms attributed to hot flashes, sleep disturbances, or other climacteric symptoms. No hard data exist to indicate whether oestrogen could be used as adjunctive therapy for other depressive disorders during the menopausal transition or postmenopausal period. The use of antidepressants is the only proven treatment at this time.

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- 1 Myers L, Dixen J, Morrisette D, *et al.* Effects of estrogen, androgen, and progestin on sexual psychophysiology and behavior in postmenopausal women. *J Clin Endocrinol Metab* 1990;**70**:1124–31.
- 2 Schmidt PJ, Nieman L, Danaceau MA, *et al.* Estrogen replacement in perimenopause-related depression: a preliminary report. *Am J Obstet Gynecol* 2000;**183**:414–20.
- 3 de Novaes Soares C, Almeida OP, Joffe H, *et al.* Efficacy of estradiol for the treatment of depressive disorders in perimenopausal women: a double-blind, randomized, placebo-controlled trial. *Arch Gen Psychiatry* 2001;**58**:529–34.
- 4 Hlatky MA, Boothroyd D, Vittinghoff E, *et al.* Quality-of-life and depressive symptoms in postmenopausal women after receiving hormone therapy: results from the Heart and Estrogen/Progestin Replacement Study (HERS) trial. *JAMA* 2002;**287**:591–7.
- 5 Bosworth HB, Bastian LA, Kuchibhatla MN, *et al.* Depressive symptoms, menopausal status, and climacteric symptoms in women at midlife. *Psychosom Med* 2001;**63**:603–8.