Estradiol and treatment of depressive symptoms

Robert K. Schneider MD
James L. Levenson MD

Revised 5-8-2002 by Robert K. Schneider MD


BACKGROUND
Depressive symptoms and somatic symptoms are common in women entering menopause. Studies of estrogen replacement for mood symptoms have shown mixed results. Issues involving the estrogen preparation, endocrinological confirmation of perimenopause, measurement of mood symptoms and loss of placebo control with changes in uterine bleeding have limited prior studies.

AIM
To determine the efficacy of estrogen replacement treatment for mood symptoms in depressive disorders in endocrinologically confirmed perimenopausal women.

METHODS
Randomized, double-blind, placebo controlled trial of women with follicle stimulating hormone > 25 IU/L and meeting criteria for a depressive disorder (i.e. major depression, dysthymia or minor depression). Patients received 17β-estradiol (100µg) transdermal patches or placebo for 12 weeks. The subjects were re-evaluated after a 4-week washout period at the conclusion of the study.
MAIN FINDINGS
Estradiol levels were significantly higher than baseline in the treatment group (P<0.001) and not in the placebo group. Remission of depressive symptoms was seen in 68% subjects treated with estradiol and 20% of the placebo group (P=0.001). There were no significant differences in the responses according to type of depressive disorder. A 50% reduction in menopausal symptoms was seen in 68% subjects treated with estradiol and 28% of the placebo group (P=0.005). After the washout period, 59% in the estradiol group maintained remission of their depressive symptoms, whereas none of the placebo responders maintained remission. Also, after washout, the treatment group showed a significant increase (P<0.001) in menopausal symptoms and the placebo group did not. Of the subjects who had remission of depressive symptoms 70% had a return of moderate-to-severe hot flushes during the washout period but remained in remission with their depressive symptoms.

CONCLUSIONS
Treatment with transdermal estrogen patches is effective for depressive symptoms in some perimenopausal women.

LIMITATIONS
The patients were recruited from a specialized outpatient clinic and this may impact generalizability of the results. The total number of subjects is small even though the authors state that this is the largest study examining the impact of estradiol on MDD. Also, 12 weeks is a relatively short time period when evaluating "remission" from depressive disorders and 4 weeks is a short period of time for assessing relapse of any symptoms.

IMPACT ON INTERNAL MEDICINE
Women going through menopause are often highly symptomatic with physical and mood symptoms. There is a growing body of evidence that indicates estrogen influences CNS functions. In prior placebo-controlled studies of
estrogen replacement, oral estrogen preparations did not show significant effect on mood. The authors suggest that transdermal estrogen provides a more rapid rise and steady level of serum estradiol than oral preparations. Still this is a small and relatively short-term study that is in need of replication in a larger community-based setting.