

## Psychopharmacology for the Clinician

The information in this column is not intended as a definitive treatment strategy but as a suggested approach for clinicians treating patients with similar histories. Individual cases may vary and should be evaluated carefully before treatment is provided.

### Is there a role for estrogen in treating depression during menopause?

Accumulating evidence suggests that some women may be at heightened risk for mood symptoms during periods of intense hormone variations, which represent a challenge to clinicians; the menopause transition (MT) is a paramount example.<sup>1</sup> The MT is often accompanied by changes in metabolism, sexuality, behaviour and overall health, including greater susceptibility to cardiovascular events, metabolic syndrome, obesity and hypertension. Given the controversy on the risks and benefits of hormone-replacement therapy (HRT) for menopause, should mental health professionals consider estrogen as part of the treatment plan?

Ms. A, a 50-year-old woman with no history of depression, reported mood swings, low energy, diminished pleasure in daily activities, increasing irritability, disrupted sleep and lack of concentration for the past year. Irregular cycles started 3 years ago, and her last menstruation was 18 months ago. She reported hot flashes and night sweats over the past 2 years and problems with her sexual functioning owing to low libido, dryness and pain during intercourse.

Ms. A's case illustrates a new onset of depression related to the MT, with co-occurrence of mood, cognitive and somatic/sexual complaints. For years HRT has been the treatment of choice for menopause-related symptoms, particularly vasomotor symptoms and sexual dysfunction. Recent studies have investigated the efficacy and safety of HRT in perimenopausal women with depression. Estrogen therapies (particularly transdermal estradiol [E2], 50–100 µg/d) have shown significant antidepressant efficacy in placebo-controlled trials including perimenopausal women.<sup>2</sup> An

age-stratified analysis of the Women's Health Initiative data revealed that cardiovascular events (death, nonfatal myocardial infarction, stroke) associated with the use of HRT were not evident in women aged 50–59 years. These analyses demonstrated a cardio-protective effect and reduced mortality attributed to estrogen when used by younger women within 10 years of the final menstruation; however, increased risk for stroke remained significant and not influenced by years since menopause, except in women aged 50–59 years.<sup>3</sup> In the absence of clear contraindications for HRT, existing data support a window of opportunity for estrogen use during the MT. For Ms. A, a trial with E2 (50–75 µg/d) led to improvement in mood, sleep and sexual complaints, and subsequent assessments ruled out the need for antidepressant use.

Ms. X, a 48-year-old woman, reported a history of mild premenstrual symptoms and a postpartum depressive episode. Her current depressive episode started 5 years ago, accompanied by irritability, sleep disturbance and headaches. Treated initially with a selective serotonin reuptake inhibitor (SSRI), she remained stable until about 6 months ago, when menstrual cycle irregularities, mood swings, anhedonia, low libido, difficulty concentrating, night sweats and diurnal hot flashes began. These new symptoms adversely impacted her sleep quality and overall social functioning.

Ms. X's case illustrates the worsening of a depressive disorder related to the MT. Preclinical studies have shown that estrogen can modulate molecular pathways involved in monoaminergic neurotransmission (serotonin, norepinephrine) that are known to regulate mood and behaviour.<sup>4</sup> Clinical trials have shown that estrogen-based therapies have antidepressant properties and augment the response to antide-

pressant agents. Ms. X had no depressive symptoms, irritability or concentration/energy problems after 12 weeks of combined use of SSRI and transdermal E2 (100 µg/d). Subsequent use of continuous progesterone (100 mg/d), required for endometrial protection, had no deleterious impact on her quality of life or adherence to treatment.

Both examples highlight the effectiveness of estrogen as a treatment option in the management of depression in perimenopausal women. Clinical data support its use as a monotherapy or adjunctive strategy to antidepressants for vasomotor, sexual and other menopause-related symptoms. Screening and management of risk factors for stroke is recommended before considering estrogen therapy, and the use of transdermal E2 is particularly advisable owing to more efficacy data for mood improvement and a more promising cardiovascular profile owing to its effects on triglycerides and C-reactive protein levels and reduced risk for venous thromboembolism.

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**References**

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