

Vasomotor Symptoms and Depression in Women, Part 2

Treatments That Cause Remission and Prevent Relapses of Major Depressive Episodes Overlap With Treatments for Vasomotor Symptoms

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Issue: Relieving vasomotor symptoms is emerging as a necessary dimension to optimal treatment of depression.

Vasomotor symptoms may be linked to changing levels of estrogen, which can affect levels of neurotransmitters and neural proteins that modulate the risk of depression in some women, thus serving as harbingers of oncoming depression or signs of incomplete recovery from a major depressive episode (MDE).¹⁻⁴ The question arises whether clinicians who normally diagnose and treat depression should also diagnose and treat vasomotor symptoms, and if so, how.

Estrogen Treatment for Vasomotor Symptoms and Perimenopausal Depression

Fluctuating estrogen levels can theoretically create monoaminergic dysfunction in the brain; when this dysregulation occurs in the hypothalamic

thermoregulatory centers, vasomotor symptoms may occur (Figure 1).¹⁻⁴

Because estrogen replacement therapy (ERT) is the recognized treatment option for vasomotor symptoms of perimenopause,³ estrogen might seem a natural therapeutic choice for perimenopausal depression as well. However, (1) many women are not willing to take estrogen for vasomotor symptoms, and most prescribers are not willing to treat long-term with estrogen due to health risks,^{1,3} which has created the need for a nonhormonal treatment for vasomotor symptoms, and (2) no type of hormonal therapy is yet approved for the treatment of perimenopausal depression, and the multitude of available formulations has long obscured any clear results, even in experimental literature. Low doses of oral estrogens or estrogens/progestins are generally not consistently effective for perimenopausal depression.⁵ Higher doses of transdermal estradiol may be effective for depression in some perimenopausal women⁶ but not often in postmenopausal women.⁷ Add to this confusion the constantly changing and controversial reports about risk-benefit ratios of ERT, and the clinician is left with an unapproved and uncertain therapy as well as possibly an unwilling patient.

Antidepressant Treatment for Perimenopausal Depression and Vasomotor Symptoms

Various psychotropic drugs are now emerging as potential treatments for vasomotor symptoms.³ For example, SSRIs show some, if inconsistent, benefit for relief of vasomotor symptoms.^{1,3} Results are generally more positive for paroxetine, classified by some as a weak SNRI and for which the noradrenergic reuptake blocking activity may have an effect.¹ Well-characterized SNRIs such as duloxetine and desvenlafaxine may show a clearer benefit for relief of vasomotor symptoms (Figure 1E),⁸⁻¹⁰ although such agents are not approved for this use. These actions might also be expected for the SNRIs venlafaxine, milnacipran, and others, although there are few or no data on treatment of vasomotor symptoms by these agents. Under investigation is whether various SNRIs have the same effect size as estrogen and whether the benefits versus the risks of SNRIs justify their use in treating vasomotor symptoms in perimenopausal women.

Summary

One of the most important contemporary issues in the treatment of depression is to treat to remission of

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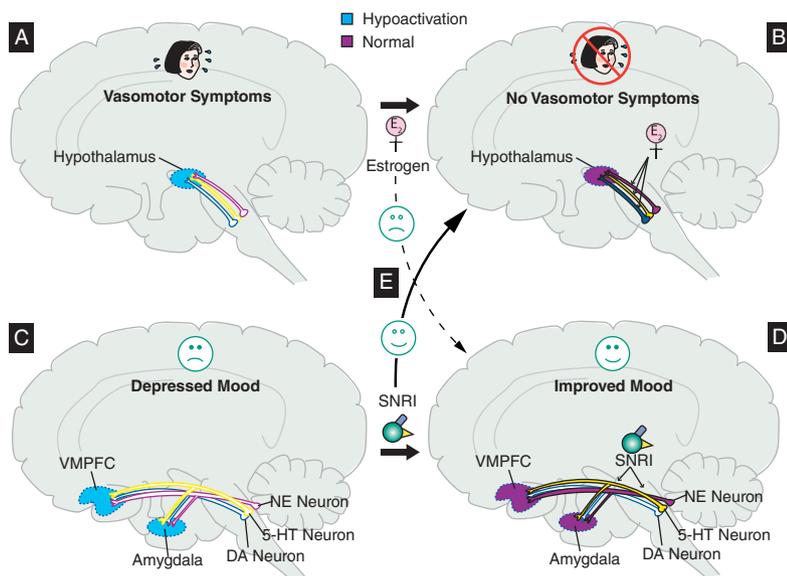
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TAKE-HOME POINTS

- ◆ In perimenopause, vasomotor symptoms may be harbingers of oncoming depression and also may signal the presence of dysregulated hormones and neurotransmitters.
- ◆ Continuing vasomotor symptoms may also signal the lack of remission and an increased risk of relapse of depression in women who otherwise appear to have resolution of the symptoms of a major depressive episode.
- ◆ For women who wish to avoid the use of estrogen to treat vasomotor symptoms, certain antidepressants, especially serotonin-norepinephrine reuptake inhibitors (SNRIs), are emerging as potential treatments not only for symptoms of depression, but also for vasomotor symptoms.

Figure 1. Effect of Estrogen and Serotonin-Norepinephrine Reuptake Inhibitors (SNRIs) on Vasomotor Symptoms and Depression^a



^aAdapted with permission from Stahl.¹

A: Fluctuating or low levels of estrogen may produce trimonoamine neurotransmitter deficiency, which can cause vasomotor symptoms if the hypothalamus is affected.

B: Administering estrogen can alleviate vasomotor symptoms.

C: Fluctuating or low levels of estrogen may produce trimonoamine neurotransmitter deficiency, which can cause depressed mood if the limbic areas are affected.

D: Actions on both serotonergic and noradrenergic systems may be responsible for the ability of SNRIs to sustain efficacy in treating depression symptoms even when estrogen levels are low or fluctuating.

E: Hormone replacement therapy has not been proven effective in the treatment of depressed mood⁵⁻⁷; however, SNRIs have shown great promise for relief of vasomotor symptoms.^{1,8-10}

Abbreviations: DA = dopamine, 5-HT = serotonin, NE = norepinephrine, VMPFC = ventromedial prefrontal cortex.

antidepressants, especially the SNRIs, are emerging to treat both depression and vasomotor symptoms. Current research is exploring the risks and benefits of this approach. ◆

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all symptoms and to prevent recurrences.¹ Increasingly, symptoms such as anxiety and pain, and now vasomotor symptoms, not classically considered diagnostic symptoms of depression, are considered closely linked to major depression and to require treatment for

true remission of an MDE in patients experiencing these symptoms in addition to the classical symptoms of depression.^{1,3} Although ERT may reduce vasomotor symptoms and even some symptoms of depression in some patients, risks are evident. Several