










Paroxetine controlled release was effective and tolerable for treating menopausal hot flash symptoms in women

Stearns V, Beebe KL, Iyengar M, *et al.* Paroxetine controlled release in the treatment of menopausal hot flashes: a randomized controlled trial. *JAMA* 2003;**289**:2827–34.

Clinical impact ratings GP/FP/Primary care ★★★★★☆☆ Endocrine ★★★★★☆☆

Q In women who are menopausal, is paroxetine controlled release (CR) effective and tolerable for treating vasomotor symptoms?

METHODS

-  **Design:** randomised placebo controlled trial.
-  **Allocation:** {concealed*}†.
-  **Blinding:** blinded {patients, healthcare providers, data collectors, outcome assessors}†.*
-  **Follow up period:** 6 weeks.
-  **Setting:** 17 sites (including urban, suburban, and rural clinics) in the US.
-  **Patients:** 165 women ≥18 years of age (mean age 54 y) who were menopausal (defined as amenorrhoea for ≥12 consecutive mo, amenorrhoea for 6 mo and meeting the biochemical criteria for menopause, or history of bilateral oophorectomy ≥6 wks before screening), experienced ≥2–3 daily hot flashes or ≥14 bothersome hot flashes/week, had discontinued hormone replacement therapy for ≥6 weeks, and had discontinued psychotropic drugs for 2–12 weeks (specified for class of medication). Exclusion criteria included active cancer, active psychiatric disorder, concurrent major depression, intolerance to selective serotonin reuptake inhibitors (SSRIs), and substance dependence.
-  **Interventions:** after a 1 week placebo run in phase, women were allocated to receive paroxetine CR, 12.5 mg/day (n=51) or 25 mg/day (n=58), or placebo (n=56) for 6 weeks.
-  **Outcomes:** self reported daily composite hot flash score, which was calculated by multiplying daily frequency and severity (minimum severity score 1, maximum severity score 4) ratings; hot flash frequency; and adverse events.
-  **Patient follow up:** 97%

*See glossary.
†Information provided by author.

MAIN RESULTS

After adjustment for age, disease history, and antioestrogen use, mean reductions from baseline in daily composite hot flash score

were greater for patients who received paroxetine CR, 12.5 mg/day (8.52, p = 0.007) or 25 mg/day (7.43, p = 0.03) than for patients who received placebo (3.82). Similarly, mean reductions from baseline in daily hot flash frequency were greater for patients who received paroxetine CR, 12.5 mg/day (3.3, p = 0.01) or 25 mg/day (3.2, p = 0.01) than for patients who received placebo (1.8). Also, adjusted mean reductions from baseline in vasomotor symptom scores (measured by the Greene Climacteric Scale) were greater for patients who received paroxetine CR, 12.5 mg/day (1.75, p = 0.005) or 25 mg/day (1.55, p = 0.02) than for patients who received placebo (0.83). The groups did not differ for rates of adverse events, which were few and primarily mild or moderate in severity.

CONCLUSION

In women who are menopausal, paroxetine controlled release was effective and tolerable for treating menopausal hot flash symptoms.

Commentary

In the wake of the Women’s Health Initiative¹, many clinicians and patients have turned to nonhormonal therapies for menopausal symptomatic relief. In this study, Stearns *et al* examine whether the use of SSRIs is beneficial in symptomatic relief of hot flashes.

In this study, paroxetine CR use is associated with decreases in hot flash frequency and composite scores in both of the study groups. It also confirms the safety of this agent, which has already been proven in the setting of depression. However, this study suffers from small sample size, high dropout rates, and a short follow up duration. Paroxetine CR was compared with a placebo control, but a hormonal therapy arm might have been more useful to determine comparability to the gold standard.

This study enrolled only women with substantial hot flashes who had a mean age of 54 years (31% were aged >54 y). Any conclusions drawn from this study should therefore be limited to this relatively narrow perimenopausal demographic. Paroxetine CR may be an important alternative for the treatment of symptomatic women with true contraindications to menopausal hormone therapy. This includes women with breast cancer (who were, unfortunately, excluded from this study), coronary artery disease, or venous thromboembolic disease. SSRIs are an interesting and promising therapeutic alternative for relief of vasomotor symptoms; however, more studies with different subsets of women and larger numbers are needed to make any definite recommendation. In addition, short term hormone replacement therapy has not yet been dismissed as a treatment option.

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1 Rossouw JE, Anderson GL, Prentice RL, *et al.* Risks and benefits of estrogen plus progestin in healthy postmenopausal women: principal results From the Women’s Health Initiative randomized controlled trial. *JAMA* 2002;**288**:321–33.

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