TOOLS FOR PRACTICE #353 | November 27, 2023

TOOLS FOR PRACTICE

PEER PATIENTS EXPERIENCE EVIDENCE RESEARCH

# Turn Down the Heat! Can non-hormonal drugs improve vasomotor symptoms in menopause?

## CLINICAL QUESTION

### Do non-hormonal medications improve menopausal vasomotor symptoms?

## BOTTOM LINE

### After 12 weeks, approximately 50-75% of women with menopausal vasomotor symptoms experience ≥50% decrease in hot flashes with selective serotonin reuptake inhibitors (SSRIs), serotonin-norepinephrine reuptake inhibitors (SNRIs) or gabapentin versus 35-60% on placebo. Placebo reduces the number of hot flashes by about 40-50%, with an additional 10-20% reduction from SSRIs, SNRIs, and gabapentin.

## EVIDENCE

- All results statistically different unless indicated.
- SSRIs (six meta-analyses, 4-11 RCTs, 547-2069 patients);[1-6] SNRIs (five meta-analyses, 2-7 RCTs, 301-3685 patients);[2-3,5,7-8] gabapentin (five meta-analyses, 2-9 RCTs, 901-3519 patients);[2,3,9-11]

clonidine (one meta-analysis, 4 RCTs, 30-198 patients).[3] When outcomes not available, largest RCTs for each drug class retrieved.
    - Hot flashes (daily):
        - SSRIs,[1] gabapentin,[3] desvenlafaxine:[12-13] Baseline 9-11;
            - Mean difference: 1-2 fewer hot flashes over placebo at 4-12 weeks.
            - Example: 3-4 hot flashes (desvenlafaxine) versus 5-6 (placebo).[12]
        - Oxybutynin (148 patients):[14] Four fewer hot flashes over placebo.
        - Clonidine:[3] One fewer hot flash over placebo.
            - No difference when breast cancer patients excluded.
    - Proportion with ≥50% reduction in number of hot flashes. Examples at 12 weeks, (unless noted):
        - Gabapentin[15] (600 patients): 73% versus 60% (placebo), number needed to treat (NNT)=8.
        - Desvenlafaxine[12] (567 patients): 68-75% versus 48% (placebo), NNT=4-5.
        - SSRIs:
            - Paroxetine[16] (614 patients) or escitalopram[17] (205 patients): 48-55% versus 36% (placebo), NNT=6-9 over 8-12 weeks.
            - Fluoxetine, citalopram (150 patients):[18] No difference versus placebo.
    - Global assessment: "Much/Very much improved" over 12 weeks:
        - Gabapentin:[15] 58% versus 44% (placebo), NNT=8.
        - Oxybutynin:[14] 73% versus 26% (placebo), NNT=2.
    - Quality of life: Versus placebo:
        - Citalopram, fluoxetine, or sertraline:[18-19] No difference.
        - Escitalopram:[20] Not clinically different.
- Limitations: Event rates not reported;[2-8,10-11] standard mean differences used (difficult to interpret clinically);[1,2,8,10-11] breast cancer patients included;[2,3,6,9-11] RCTs industry funded.[13-16,18-19]

## CONTEXT

- Guidelines:
    - First-line: Hormone therapy; second-line: SSRIs, SNRIs, or gabapentin.[21]
- Hormone therapy:
    - Versus placebo: ~18 fewer hot flashes/week (mostly estradiol 1-2mg).[22]
    - Versus gabapentin: 1 fewer hot flash/day with hormone therapy.[10]
    - Versus venlafaxine: RCT underpowered to compare agents for efficacy outcomes.[23]
        - Patient satisfaction: 70% versus 51% venlafaxine.
- Dosing (daily):[21] Paroxetine 10-25mg, desvenlafaxine 100-150mg, gabapentin 900-2400mg.

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## AUTHORS


**Ashley Domingues,** PharmD Candidate
**Émélie Braschi,** MD PhD,
**Samantha S Moe,** PharmD ACPR

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