

## Effect of escitalopram on hot flash interference

### BACKGROUND:

- Hot flash interference is an essential factor in women's quality of life at menopause.
- Currently, the only approved medications for vasomotor symptoms in menopausal women are menopausal hormone therapy.
- Evidence for the efficacy of selective serotonin reuptake inhibitors in alleviating vasomotor symptoms is growing.

### OBJECTIVE:

- To estimate the effect of escitalopram (10-20mg/day) versus placebo for reducing hot flash interference in daily life and understand correlates and predictors of reductions in hot flash interference, a key measure of quality of life.

### METHODS:

- **Design:** Multisite, randomized, placebo-controlled double blind clinical trial; Duration: 8 weeks
- **Inclusion criteria:** Women aged 40-62 years, postmenopausal ( $\geq 12$  months since the last menstrual period or bilateral oophorectomy) or in the late menopausal transition (amenorrhea  $\geq 60$  days in the past year), in good general health. Also at least 28 hot flashes or night sweats per week and recorded on daily diaries for 3 weeks; hot flashed or night sweats rated as bothersome or severe on 4 or more days per week; and hot flash/night sweat frequency in week 3 did not decrease by more than 50% from the mean weekly levels in weeks 1 and 2. Criteria were for overall total hot flashes (daytime plus nighttime).
- **Exclusion criteria:** Psychotropic medications or any hot flash treatments including herbals and OTCs in the past 30 days, hormone therapy, hormonal contraceptives, selective estrogen receptor modulators or aromatase inhibitors in the past 2 months; current severe medical illness or major depressive episode, drug or alcohol abuse in the past year, suicide attempt in the past 3 years, lifetime diagnosis of bipolar disorder or psychosis; uncontrolled hypertension, history of endometrial or ovarian cancer; or myocardial infarction, angina, cerebral vascular events, or other preexisting medical conditions.
- **Primary Outcome Measure:** To estimate the effect of escitalopram relative to placebo for reducing hot flash interference using the Hot Flash Related Daily Interference Scale.
- **Secondary Outcome Measure:** Correlations between hot flash interference and daytime and nighttime hot flash frequency, severity, bother, and the number of flash-free days and flash-free nights.
- 205 patients received either escitalopram 10mg (n=104) or placebo (n=101) once daily with follow-up at 4 and 8 weeks. At week 4, those not achieving 50% fewer hot flashes were increased to two pills daily (20mg/day escitalopram or 2 pills placebo/day).
- 90% power with alpha at 0.025 and 0.52 effect size.
- Data handling method was intent to treat.

### RESULTS:

- 96 patients completed the study in the escitalopram arm and 88 patients in the placebo arm.
- **Primary Outcome Measure:** Escitalopram significantly reduced hot flash interference during the course of the trial compared with the placebo after adjusting for race, site, and baseline

interference ( $P=.012$ ; effect size=0.15). The mean hot flash interference score was reduced 18 points in the escitalopram group or 6.0 points more in the escitalopram group compared with the placebo group at week 4 and 3.4 points more at week 8.

- Mean (95% CI) difference at baseline = 1.3 (-8.1 to 5.5)
- Mean (95% CI) difference at 4 week follow-up = -6.0 (-12.0 to 0.1)
- Mean (95% CI) difference at 8 week follow-up = -3.4 (-10.1 to 3.2)
- **Secondary Outcome Measure:** Reductions in hot flash interference were significantly correlated with reductions in daytime and nighttime hot flash frequency, severity, and bother. Reductions in hot flash interference were also significantly correlated with more flash-free days but not with flash-free nights. The greatest absolute correlation value was between hot flash interference and daytime hot flash severity ( $r=0.42$ ), followed by daytime bother ( $r=0.37$ ).
- **Author's conclusion:** Escitalopram (10-20mg/day) for 8 weeks improves women's quality of life and this benefit did not vary by demographic, clinical, mood, sleep, or hot flash variables.

#### STRENGTHS:

- Randomized, placebo-controlled, double blind study
- Inclusion and exclusion criteria were well-defined and allowed results to be extrapolated

#### LIMITATIONS:

- Equal numbers of African-American and white women were included in this study, but findings may not be generalizable to other racial or ethnic groups.
- The women studied were community based volunteers.
- Short duration
- No data provided to account for compliance or adverse events
- SSRI was stopped at the end of the study, possibility for withdrawal effect.
- There was no power given for the secondary measures, which makes it difficult to assess whether or not error could have occurred.

#### CONCLUSIONS:

- The correct outcomes were measured for this type of study; however, the results were not interpreted appropriately by the authors. The authors concluded that the results were statistically significant for a HFRDIS total, in which they did not give the related values for this. The results for the difference between treatment groups in each individual stage (baseline, week 4, week 8) were not statistically significant because the mean score, with a 95% CI, included the value, zero. The study was also not clinically significant, in which the authors concluded that it was. These small changes in the HFRDIS scores are not enough to prove usefulness in clinical practice.
- The authors stated that the data handling method used was intent to treat, although it was actually exclusion of subjects, because the results for subjects who did not complete their diaries were not analyzed at the end of study.
- There were no adverse events or compliance reporting which could have skewed the results in a favorable or negative way.
- This therapy has the potential to be effective in the future due to minor favorable results that have been reported and also due to its cost, recently becoming generic, but further research is needed.
- Future research: In the future, it would be beneficial to extend the study duration to achieve the full effectiveness of escitalopram. Also, including compliance monitoring, checking for adverse events, and evaluating for unblinding could help strengthen the study.