Short-Term Efficacy and Safety of Desvenlafaxine in a Randomized, Placebo-Controlled Study of Perimenopausal and Postmenopausal Women with Major Depressive Disorder

BACKGROUND

- The risk for being depression has been reported to increase during menopause.
- Little is known about the efficacy of antidepressants in peri- and postmenopausal women.
- A large, randomized, prospective study is needed in this specific population.

OBJECTIVE

- The objective of this study was to evaluate short-term efficacy and safety of women with MDD who are perimenopausal and postmenopausal.

METHODS

- **Design:** Multicenter, double-blind, randomized, placebo-controlled trial. Duration: 8 weeks.
- **Inclusion criteria:** Perimenopausal or postmenopausal women aged 40 to 70 years old, meeting the DSM IV criteria for MDD, single or recurrent episode, without psychotic features, and depressive symptoms for at least 30 days prior to screening.
- **Exclusion criteria:** Patients could not have received desvenlafaxine before, could not have a hypersensitivity to venlafaxine, could not have a significant suicide risk, could not be pregnant or breast-feeding. Patients were also excluded if within 12 months they had psychoactive abuse or dependence, manic episodes, post-traumatic stress disorder, OCD, or a clinically important personality disorder or a lifetime diagnosis of a psychotic disorder or bipolar disorder. Patients could not participate in the study if they had depression due to an organic mental disorder, had a history of seizures, or had a clinically important condition such as uncontrolled hypertension or unstable angina. If patients had received formal cognitive-behavioral therapy or interpersonal therapy 30 days or less from baseline, they were excluded. If patients had used one of the following treatments, they were also excluded: hormone products within 4 weeks to 6 months before baseline (depending on the route of administration of the hormone), antidepressants, anxiolytics, sedative hypnotics (other than zaleplon, eszopiclone, or zolpidem), serotonin precursors, psychotropic drugs, non-psychotropic drugs with psychotropic effects, herbal products intended to treat anxiety, insomnia, or depression within 7 days before baseline. Also excluded were patients that had received electroconvulsive therapy or formal psychotherapy within 6 months before baseline.
- **Primary Outcome Measure:** Change from baseline in 17-item HDRS total score.
- **Secondary Outcome Measures:** HDRS17 clinical response rate, HDRS17 remission rate , CGI-I, MADRS, HARS, CGI-S, EQ-5D, MRS, SDS, QIDS-SR, MADRS response rate, and CGI-I response rate

RESULTS

- **Primary Outcome Measure:** The Hamilton Depression Rating Scale decrease in mean score was 8.33 points in the placebo group (SD= 7.3) and 12.64 points in the desvenlafaxine group (SD= 7.2).
- **Secondary Outcome Measures:**
    - The treatment effect for desvenlafaxine in perimenopausal women was a decrease of 4.07 points (95% CI, -6.77 to -1.37).
    - The treatment effect for desvenlafaxine in postmenopausal women was a decrease of 3.27 points (95% CI, -5.07 to -1.47).
    - The remission rates (score less than 7) for desvenlafaxine were significantly higher than placebo (38.2% vs 22.4%, p = .008)

- MADRS total score was decreased by 11.77 points in the placebo group (SD= 10.3) and 18.21 points (SD= 10.22) in the desvenlafaxine group.
- MRS scores were decreased by 6.11 points in the placebo group (SD= 7.22) and 8.84 points in the treatment group (SD = 7.23) p=.003
- For the CGI-I test, a significantly higher percentage of women in the treatment group scored a 1 (very much improved) or a 2 (much improved) compared with placebo (67.7% vs 41.2%, p <.001).

- **Author's Conclusion:**
  - Desvenlafaxine-treated patients achieved significantly greater outcomes than placebo on the HDRS17 total score, as well as all of the secondary outcome measures.

STRENGTHS

- Power was adequate for the intention-to-treat analyses
- Results were statistically significant

LIMITATIONS

- Compliance to study medications was not assessed
- Study duration was too short
- Large number of exclusion criteria limit ability to extrapolate data to general population
- Large variance at baseline for duration of depression in the placebo group
- Much of the discussion is biased toward desvenlafaxine, making it appear as though nothing else will help perimenopausal and postmenopausal women's depression

CONCLUSION

- Desvenlafaxine seems to have a higher incidence of adverse effects with only a modest benefit versus placebo in perimenopausal and postmenopausal women for the treatment of MDD.
- Desvenlafaxine should not be recommended for treatment of MDD in peri- and postmenopausal women based on this study.
- Venlafaxine is a racemic mixture which is currently available as a generic. Further study is needed to determine if the same results obtained with desvenlafaxine would be seen with venlafaxine.
- A study which focuses specifically on desvenlafaxine and vasomotor symptoms would be needed before a true correlation between desvenlafaxine and reduced hot flashes can be made.

Reference: Kornstein SG, Jiang Q, Reddy S, Musgnung JJ, and Guico-Pabia CJ. Short-term efficacy and safety of desvenlafaxine in a randomized, placebo-controlled study of perimenopausal and postmenopausal women with major depressive disorder. J Clin Psychiatry. 2010 Aug;71(8):1088-96.

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