Venlafaxine offers no benefit over sertraline and is less well tolerated in depressed nursing home residents


**Q** What are the relative benefits and risks of sertraline and venlafaxine in depressed nursing home residents?

**METHODS**

- **Design:** Randomised controlled trial.
- **Allocation:** Unclear.
- **Blinding:** Double blind.
- **Follow up period:** 10 weeks.
- **Setting:** 13 nursing homes, USA; time period not stated.

**Patients:** 52 nursing home residents (mean age 82.5 years) with depression (DSM-IV). Main inclusion criteria: significant dysphoria (Geriatric Depression Scale score >10 and/or Hamilton Rating Scale for Depression (HAM-D) item 1 rating >2); diagnosis of major depressive episode, minor depression, dementia with depression, or dysthymic disorder, or 17 item HAM-D score >12; symptom duration >1 month. Exclusions: psychosis; substance abuse; previous manic/schizophrenia; psychotropic drugs in previous 2 weeks; prior adverse reaction or non-response to sertraline or venlafaxine; communication disorders impeding assessment; dangerous weight loss; suicidality; unstable medical comorbidity; life expectancy <6 months. Participants received placebo for 1 week, those still meeting inclusion but not exclusion criteria were randomised.

**Intervention:** Sertraline (titrated up to maximum of 100 mg/day) or immediate release venlafaxine (titrated up to maximum of 150 mg/day) for 10 weeks.

**Outcomes:** Depressive symptoms (21 item HAM-D score), adverse events.

- **Patient follow up:** 90%.

**MAIN RESULTS**

At 10 weeks, there were no significant differences in improvement of symptoms between groups (mean improvement in HAM-D score: 8 with sertraline v 4.6 with venlafaxine; p = 0.069; intention to treat analysis). Sertraline was associated with significantly fewer withdrawals due to serious adverse events or side effects than venlafaxine (5/25 (20%) with sertraline v 12/27 (44%) with venlafaxine; Fisher’s exact p = 0.019).

**CONCLUSIONS**

There was no evidence for immediate release venlafaxine having greater efficacy than sertraline in depressed nursing home residents. This result may have been because the study was underpowered to detect a difference. However, venlafaxine was less well tolerated than sertraline in this population.

---

**Commentary**

The majority of the relatively few antidepressant randomised controlled trials (RCTs) in the elderly involve outpatients, aged about 70 years, who are ambulatory and relatively healthy. The larger trials comparing SSRIs antidepressants with placebo in these “young” old outpatient populations show a modest efficacy effect size. Adverse events over 6–12 week trial durations tend to be mild and comparable to those observed in trials of middle aged depressed people. Notably, only one trial has attempted to assess long term efficacy or prophylaxis compared to placebo.

In contrast, this trial was conducted in a very old, medically frail population, with significant depressive symptoms but heterogeneous diagnoses. Nearly half were cognitively impaired, some to a moderate degree. This is the milieu in which the Penn group’s trial needs to be assessed.

As the authors acknowledge, the trial lacks a placebo group that would have established “assay sensitivity” or external validity. In the absence of evidence that either sertraline or venlafaxine is more effective than placebo in this medically frail population, the trial can provide evidence only for relative overall effectiveness of sertraline compared with venlafaxine.

There is an obvious need for specific research on the relevant and vulnerable elderly patients. Without such evidence, physicians prescribe by generalising from trials of younger patients and by conforming to expert opinion often provided without evidence. For example, US experts liberally asserted that venlafaxine would be a strong second choice as an antidepressant yet the evidence here suggests greater caution. The extent of adverse events with venlafaxine in this trial is concerning, but the sample is too small to discover the circumstances in which they occur.

Results of one trial will not change clinical practice. There is prevailing clinical belief (that is, equipoise) that antidepressants are effective and should be given to patients such as those included in this trial, so much so that as the authors stated, a placebo controlled trial is difficult to do. Until further RCTs in this population have been conducted, the efficacy and overall effectiveness of antidepressants in this group of patients remains uncertain.

Lon S Schneider, MD
Professor of Psychiatry, Neurology, and Gerontology, University of Southern California Keck School of Medicine, Los Angeles, USA

---