Review: Venlafaxine is more effective than selective serotonin-reuptake inhibitors for depression

Smith D, Dempster C, Glanville J, Freemantle N, Anderson I. **Efficacy and tolerability of venlafaxine compared with selective serotonin reuptake inhibitors and other antidepressants: a meta-analysis.** Br J Psychiatry. 2002 May;180:396-404.

QUESTION

In patients with depressive disorders, is venlafaxine more effective and tolerable than other antidepressants?

DATA SOURCES

Studies were identified by searching MEDLINE, EMBASE/Excerpta Medica, BIOSIS, PsycLIT, National Research Register, Health Systematic Reviews, DARE, Cochrane Controlled Trials Register, and Current Controlled Trials. Reference lists were hand searched, and authors and study sponsors were contacted.

STUDY SELECTION

2 reviewers independently selected randomized, double-blind, controlled trials that compared venlafaxine with another antidepressant for the treatment of depression. Disagreements were resolved by discussion.

DATA EXTRACTION

Data were extracted on patient age and sex, patient selection criteria, drug doses and regimens, quality of study methods, length of follow-up, and outcomes (depression severity, response [≥ 50% improvement from baseline], remission [depression rating scale score below predefined threshold], and total dropouts).

MAIN RESULTS

32 studies (5562 patients) were included. Sample sizes ranged from 28 to 382 patients (mean 179 patients). The length of follow-up ranged from 4 to 48 weeks (mean 10 wk). When studies were pooled, the mean severity of depressive symptoms was lower for venlafaxine than for other antidepressants (Table). When grouped by drug class, venlafaxine was more effective than selective-serotonin reuptake inhibitors (SSRIs) but did not differ from tricyclic agents (TCAs) or other drugs (Table). A similar treatment effect was seen for response and remission rates (Table). Venlafaxine did not differ from other antidepressants for total dropout rates.

CONCLUSIONS

In patients with depressive disorders, venlafaxine is more effective than selective-serotonin reuptake inhibitors. Dropout rates do not differ between venlafaxine and other types of antidepressants.

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Venlafaxine vs other antidepressants for depressive disorders at mean follow-up of 10 weeks*

Outcomes	Comparator drug	Number of trials	Pooled effect size (95% CI)	
Mean depression severity	TCA	7	–0.13 (–0.33 to 0.09)†	
	SSRI	19	–0.17 (–0.27 to –0.08)	
	Other (mirtazapine, trazodone)	3	–0.09 (–0.42 to 0.23)†	
	Overall	29	–0.14 (–0.22 to –0.07)	
			Pooled odds ratio (CI)	**NNT (CI)**
Response rates	TCA	8	1.29 (0.89 to 1.85)†	
	SSRI	17	1.26 (1.02 to 1.58)	
	Other (mirtazapine, trazodone)	3	1.28 (0.43 to 4.31)†	
	Overall	28	1.27 (1.07 to 1.52)	19 (11 to 63)
Remission rates	TCA	1	1.03 (0.46 to 2.32)†	
	SSRI	16	1.43 (1.21 to 1.71)	
	Other (mirtazapine)	1	0.69 (0.33 to 1.43)†	
	Overall	18	1.36 (1.14 to 1.61)	14 (9 to 29)

*SSRI = selective-serotonin reuptake inhibitor; TCA = tricyclic agent. Other abbreviations defined in Glossary. Response defined as ≥ 50% improvement from baseline. Remission defined as depression rating scale score below a predefined threshold.
†Not significant.

COMMENTARY

Clinical guidelines and systematic reviews typically hold that available antidepressants are equally efficacious and effective. The meta-analysis by Smith and colleagues, however, found that venlafaxine led to greater reduction in depressive symptoms and greater probability of good clinical outcome than did prescription of other antidepressants in general or SSRI antidepressants in particular. Because the meta-analysis included data from traditional efficacy studies, some questions remain regarding generalizability to everyday practice.

First, did the selection process for these efficacy trials create an inadvertent bias in favor of venlafaxine? Given current medication-use patterns, previous unsuccessful treatment with SSRI drugs may have been more common than unsuccessful treatment with venlafaxine.

Second, does the Hamilton Depression Rating Scale (HDRS) measure the treatment effects that matter most to patients? The authors' point would be stronger if other measures (such as patients' global ratings of improvement or quality-of-life measures) also showed an advantage for venlafaxine. The specific symptoms included in the HDRS (e.g., insomnia rather than hypersomnia) might bias comparisons of venlafaxine with other classes of drugs.

Third, how might results be affected by the treatment structure of a randomized efficacy trial? Such trials typically limit dose adjustment and prohibit medication switches. Data collection ignores patients discontinuing protocol treatment. In actual practice, switching antidepressant medication is common and not an indication of treatment failure. Practicing clinicians ask, "Which medication should I try first?" rather than, "Which medication must I stick with regardless of the outcome?"

As the authors correctly point out, their finding of an efficacy advantage for venlafaxine should be confirmed by subsequent studies, including more generalizable patient populations, a broader range of outcome measures, and more typical treatment conditions. Pending such studies, this meta-analysis strengthens previous suggestions that venlafaxine offers some efficacy advantage over SSRI antidepressants.

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