

Sildenafil improved erectile dysfunction and quality of life in men with comorbid mild-to-moderate depression

Seidman SN, Roose SP, Menza MA, Shabsigh R, Rosen RC. Treatment of erectile dysfunction in men with depressive symptoms: results of a placebo-controlled trial with sildenafil citrate. *Am J Psychiatry*. 2001 Oct;158:1623-30.

QUESTIONS

In men with erectile dysfunction (ED) and mild-to-moderate depression, does depression affect ED treatment response to sildenafil and does improvement in ED affect depression?

DESIGN

Randomized {allocation concealed*}†, blinded {patients, clinicians, data collectors, and outcome assessors}‡,* placebo-controlled trial with 12-week follow-up.

SETTING

20 urology clinics in the United States.

PATIENTS

152 men (mean age 56 y) who had ED for ≥ 6 months (mean duration 6 y); a stable relationship with a female partner for ≥ 6 months; a *Diagnostic and Statistical Manual of Mental Disorders, 4th edition (DSM-IV)*, diagnosis of depressive disorder not otherwise specified; and a Hamilton Depression Rating Scale score of ≥ 12 . Exclusion criteria included presence of another axis I psychiatric disorder, current use of nitrates or any antidepressant medication, and abnormal serum hormone levels. 89% of patients were included in the analysis.

INTERVENTION

74 men were allocated to flexible-dose (25 to 100 mg) sildenafil begun at 50 mg, and 78 were allocated to matching placebo, both to be taken 1 hour before sexual activity.

MAIN OUTCOME MEASURES

Changes in sexual function, depressive symptoms, quality of life, and adverse effects.

MAIN RESULTS

Analysis was by intention to treat. More patients in the sildenafil group were classified as treatment responders (improvement in erections and ability to have sexual intercourse and a score of ≥ 21 on the erection function domain of the International Index of Erectile Function scale) than were patients in the placebo group (Table). Improvement in ED was highly correlated with improvement in depressive symptoms and quality of life, regardless of treatment type (76% of ED

responders vs 14% of ED nonresponders achieved depression remission). Treatment-related adverse effects occurred in more patients who received sildenafil than placebo (47% vs 13%, { $P < 0.001$ }‡).

CONCLUSIONS

In men with erectile dysfunction and mild-to-moderate depression, sildenafil was associated with improved erectile dysfunction (ED). Improvement in ED was associated with improvement in depressive symptoms and quality of life.

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*See Glossary.

†Information provided by author.

‡ P value calculated from data in article.

Sildenafil vs placebo for erectile dysfunction and mild-to-moderate depressive illness at 12 weeks[§]

Outcome	Sildenafil	Placebo	RBI (95% CI)	NNT (CI)
Treatment response	73%	14%	409% (191 to 830)	2 (2 to 3)

[§]Abbreviations defined in Glossary; RBI, NNT, and CI calculated from data in article.

||Improvement in erections and ability to have sexual intercourse and a score of ≥ 21 on the erection function domain of the International Index of Erectile Function scale.

COMMENTARY

The study by Seidman and colleagues does not advocate sildenafil as treatment for primary mild-to-moderate depression. Rather, it adds to the clinical context and options available when approaching the common comorbidity of ED and mild-to-moderate depression. Although the study sets out to show that sildenafil can effectively treat ED in men with mild-to-moderate depression, it also sheds some light on the question of "Which is first, mild-to-moderate depression or ED?" By showing that alleviation of ED results in improved mild-to-moderate depression and better quality of life, the study generates more questions: Which should be treated first, mild-to-moderate depression or ED? Should they be treated concomitantly? What happens after 12 weeks? Do these findings apply to patients with major depressive disorder?

This study has some limitations. It was only 12 weeks in duration. Although the completion rates were relatively high (88% [sildenafil] and 77% [placebo]), the dropouts were not adequately accounted for, and of the 152 patients who received ≥ 1 dose of study medication, 16 were not assessed after randomization.

Use of sildenafil comes at a price. Aside from the cost of the medication, the difference in the rate of side effects was statistically significant

(47% [sildenafil] vs 13% [placebo]). The most common side effects (flushing, headache, dyspepsia, colored tinges, and increased perception of brightness of lights) were generally mild-to-moderate and transient; the higher completion rate for sildenafil implies tolerability. No deaths were reported.

A growing number of symptom clusters (e.g., social phobia, post-traumatic stress disorder, and generalized anxiety disorder) is being treated with antidepressant pharmacotherapy. This study reminds us that not all symptom clusters are primary and that there is need and value in evaluating for root issues. Maintaining "secondary" depression in assessment differentials, then considering and treating causes (ED, lack of sleep or exercise, alcohol, drugs [prescribed or otherwise], hormones, or domestic violence), can be therapeutic.

In men similar to those studied, one can safely consider closely followed primary treatment of ED with sildenafil.

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