Sildenafil reduced antidepressant-associated sexual dysfunction in men with remitted major depressive disorder

Nurnberg HG, Hensley PL, Gelenberg AJ, et al. **Treatment of antidepressant-associated sexual dysfunction with sildenafil: a randomized controlled trial.** JAMA. 2003;289:56-64.

QUESTION

In men with major depressive disorder (MDD) in remission, is sildenafil citrate effective for sexual dysfunction associated with use of selective and nonselective serotonin-reuptake inhibitor (SRI) antidepressants?

DESIGN

Randomized (allocation concealed*), blinded (patients, clinicians, {data collectors, outcome assessors, data analysts, and monitoring committee}†),* controlled trial with 6-week follow-up.

SETTING

3 outpatient medical centers in New Mexico, Arizona, and Massachusetts, USA.

PATIENTS

90 men who were 18 to 55 years of age (mean age 45 y) and had MDD in remission; were taking a selective or nonselective SRI for ≥ 12 weeks and were on a stable dose for ≥ 6 weeks; and had antidepressant-associated sexual dysfunction (AASD) as defined by *DSM-IV* criteria for ≥ 4 weeks, with satisfactory sexual function before the onset of depression or antidepressant therapy. Exclusion criteria included anatomical penile deformity; sexual disorder other than AASD; spinal cord injury; uncontrolled psychiatric disorder; or complicated diabetes or other comorbid conditions that might make sildenafil ineffective or unsafe. 84% of patients completed all baseline and 6-week assessments.

INTERVENTION

Men were allocated to sildenafil, 50 mg ($n = 45$), or matching placebo ($n = 45$). They were instructed to make ≥ 2 attempts at sexual activity per week and to take 1 tablet 1 hour before anticipated sexual activity, but not more than once daily.

MAIN OUTCOME MEASURES

Main outcome was score on the Clinical Global Impression Scale adapted for Sexual Function (CGI-SF). Secondary outcomes were scores on the International Index of Erectile Function (IIEF), the Arizona Sexual Experience Scale (ASEX), the Massachusetts General Hospital—Sexual Functioning Questionnaire (MGH-SFQ), and the Hamilton Rating Scale for Depression (HAM-D); and adverse effects.

MAIN RESULTS

Men in the sildenafil group had greater improvement on the CGI-SF, IIEF, ASEX (5 of 5 items), MGH-SFQ (4 of 5 items), and the HAM-D than did men in the placebo group. More men in the sildenafil group had CGI-SF scores ≤ 2 (much/very much improved) than did men in the placebo group (Table). Men in the sildenafil group had an increased risk for headache (Table).

CONCLUSION

Sildenafil reduced sexual dysfunction associated with use of selective or nonselective serotonin-reuptake inhibitors in men with remitted major depressive disorder.

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*See Glossary.

†Information provided by author.

Sildenafil vs placebo for sexual dysfunction associated with selective or nonselective serotonin-reuptake inhibitors in men with remitted major depressive disorder‡

Outcomes at 6 wk	Sildenafil	Placebo	RBI (95% CI)	NNT (CI)
CGI-SF score ≤ 2 (much/very much improved)	55%	4.4%	1127% (256 to 4437)	2 (2 to 3)
			RRI (CI)	NNH (CI)
Headache	40%	9.8%	315% (64 to 1010)	4 (3 to 8)

‡CGI-SF = Clinical Global Impression Scale adapted for Sexual Function. Other abbreviations defined in Glossary; RBI, RRI, NNT, NNH, and CI calculated from data in article.

COMMENTARY

If we ask our patients with depression about sexual dysfunction, we can expect many to admit that they have it, even if they don't volunteer the information. If we ask at the time the diagnosis of depression is made, we can expect 30% to 70% to report a current problem (1). If drug therapy is chosen, we can expect some patients to develop sexual dysfunction during therapy, either from depression or because of the drugs used (AASD). Because of varying study methods, the true rate of AASD is uncertain. It seems clear, however, that the rates are substantial and contribute to poor adherence (2).

For patients who respond poorly to antidepressants and develop AASD, changing to an antidepressant with a lower rate of sexual dysfunction, such as buproprion, nefazodone, or mirtazapine (3), is a logical option. For patients who respond well to antidepressant treatment, reducing the dose may decrease adverse effects (3). However, this should be done cautiously because trials evaluating continuation treatment have shown a 70% reduction in relapse rates when using the same dose at which the patient initially responded (4). A third option, as was done in this trial, is to add an adjunctive medication to address the adverse effect.

The trial by Nurnberg and colleagues was of good quality, with low risk for systematic bias. It showed that sildenafil was highly effective for AASD in men who were otherwise in good health and had normal sexual function before the onset of depression or antidepressant treatment. Erectile function, arousal, orgasm, and intercourse satisfaction were improved. Almost 80% of men required 100 mg of sildenafil to achieve these results. Neither sample size nor study duration was sufficient to determine if the positive effects on sexual function improved treatment adherence, a critical issue that deserves further study. Based on this trial, sildenafil can be recommended for men with AASD. Effective treatments for women with AASD are needed.

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