August 2002 (Vol. 51, No. 8)

FROM THE FAMILY PRACTICE INQUIRIES NETWORK

What are the treatment options for SSRI-related sexual dysfunction?

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EVIDENCE-BASED ANSWER

Substituting bupropion, nefazodone, or mirtazapine is beneficial. (Grade of recommendation: B, randomized controlled trials [RCTs].) Augmentation therapy with amantadine, bupropion, and buspirone is no better than placebo. (Grade of recommendation: B, RCTs.) Augmentation therapy with multiple other agents may be beneficial. (Grade of recommendation: D, open-label nonrandomized studies, case series, and case reports.) SSRI "drug holidays" may also be effective (**Table 1**). (Grade of recommendation: D, open-label nonrandomized studies.)

Summary of treatment options for SSRI-induced sexual dysfunction

Strategy	Drugs considered	RCT data	Other data
Switch therapy	Bupropion SR, bupropion, mirtazapine, nefazodone	Nefazodone effective	All agents effective in nonrandomized open-label trials
Augmentation	Buspirone, amantadine, bupropion, cyproheptadine, dextroamphetamine, granisetron, ginkgo biloba, methylphenidate, mirtazapine, nefazodone, pemoline, sildenafil, yohimbine	Small, transient effect with high-dose buspirone.	Other RCT with buspirone, amantadine, and bupropion showed no difference vs placebo. Most agents effective in nonrandomized open-label trials, case-series, or case reports. Placebo effect unknown
Drug holiday	Fluoxetine, paroxetine, sertraline	None available	Improvement in 2 of 4 weekends for sertraline and paroxetine only

EVIDENCE SUMMARY

SSRI-related sexual dysfunction may be dose dependent and diminish with time, but these aspects have not been evaluated prospectively. Data suggest that bupropion, nefazodone, and mirtazapine have little to no effect on sexual functioning.[1] Changing from SSRIs to one of these agents may alleviate SSRI-induced sexual dysfunction. In a randomized double-blind study, patients experiencing sexual dysfunction on sertraline improved when switched to nefazodone 400 mg daily.[2] Additional open-label nonrandomized studies of all 3 agents suggest improved sexual functioning in 60% to 85% of patients with little to no loss of antidepressant efficacy.[1,3,6] The potential for placebo effects makes interpreting these open-label trials more difficult.

Three augmentation therapies have been tested in double-blind placebo-controlled trials. In the first, buspirone augmentation resulted in a statistical improvement in sexual functioning at weeks 2 and 3 of therapy, but not at weeks 1 and 4 (mean dose 48.5 mg per day).[7] In the second, adding buspirone 20 to 30 mg per day, amantadine 50 to 100 mg per day, or placebo resulted in equal improvement in women's sexual function.[8] Finally, in a third trial, adding bupropion or placebo showed equal improvement in sexual function.[9] Multiple other agents have been tested in open-label nonrandomized studies, case series, and case reports. Most showed a beneficial effect, but results must be interpreted with caution. One open-label nonrandomized study of weekend "drug holidays" showed no benefit for fluoxetine and inconsistent results for paroxetine and sertraline.[10]

RECOMMENDATIONS FROM OTHERS

Tertiary literature sources recommend the strategies described above.[11]

Clinical Commentary by Michael Fisher, MD, additional references, search strategy, and detailed evidence table at **http://www.fpin.org**.

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