Clinical Inquiries
FROM THE FAMILY PRACTICE INQUIRIES NETWORK

Which Antidepressant Is Best to Avoid Sexual Dysfunction?

Searchable Question

In patients being treated for depression, which antidepressants have a low risk of sexual side effects?

Evidence-Based Answer

Bupropion (Wellbutrin), nefazodone (Serzone), amitriptyline (Elavil), and moclobemide (Manerix, a reversible inhibitor of monoamine oxidase type A not available in the United States) have been shown to cause less sexual dysfunction than selective serotonin reuptake inhibitors (SSRIs). [Strength of recommendation: B, based on individual randomized controlled trials (RCTs)] Among SSRIs, fluvoxamine (Luvox) may cause less sexual dysfunction than sertraline (Zoloft). [Strength of recommendation: B, single RCT] No other differences between or within classes of antidepressants have been demonstrated in RCTs.

Evidence Summary

The incidence of sexual side effects between different antidepressants in adults with depressive or anxiety disorders has been reported by 25 RCTs, most of which were included in two recent descriptive systematic reviews.1,2 [References 1 and 2--Evidence level 1A] Bupropion led to less sexual dysfunction (or to more sexual satisfaction) than sertraline or fluoxetine in four trials. The number needed to harm (NNH), that is, the number of patients who have to take the drug for one patient to experience sexual dysfunction, ranged from two to 17, depending on the type of dysfunction.1,2 Nefazodone led to less sexual dysfunction (or to more sexual satisfaction) than sertraline in two trials (NNH: two to seven).1-3 [Reference 3--Evidence level 1B] Moclobemide led to less sexual dysfunction than four SSRIs in one trial (NNH: five) and to greater sexual desire than doxepin (Adapin) in one trial (number needed to treat: eight).2-4 [Reference 4--Evidence level 1B] The accompanying table1-4 summarizes the different adverse sexual effects and the agents that cause them.

<p>| Significantly Different Adverse Sexual Effects Caused by Various Antidepressants |</p>
<table>
<thead>
<tr>
<th>Outcome</th>
<th>Agents</th>
</tr>
</thead>
<tbody>
<tr>
<td>Increased sexual desire</td>
<td>Moclobemide* (Manerix) &gt; doxepin (Adapin)</td>
</tr>
<tr>
<td>Diminished sexual desire</td>
<td>Fluoxetine (Prozac) &gt; bupropion (Wellbutrin); sertraline (Zoloft) &gt; nefazodone (Serzone)</td>
</tr>
<tr>
<td>Sexual arousal disorder</td>
<td>Sertraline, fluoxetine &gt; bupropion; sertraline &gt; nefazodone</td>
</tr>
<tr>
<td>Ejaculatory abnormality</td>
<td>Sertraline &gt; nefazodone</td>
</tr>
<tr>
<td>Orgasm dysfunction, male</td>
<td>Sertraline &gt; bupropion</td>
</tr>
<tr>
<td>Orgasm dysfunction, female</td>
<td>Sertraline &gt; bupropion</td>
</tr>
<tr>
<td>Orgasm dysfunction, total</td>
<td>Sertraline, fluoxetine &gt; bupropion</td>
</tr>
<tr>
<td>Sexual dysfunction, male</td>
<td>Sertraline &gt; amitriptyline (Elavil)</td>
</tr>
<tr>
<td>Sexual dysfunction, female</td>
<td>Sertraline &gt; nefazodone</td>
</tr>
<tr>
<td>Sexual dysfunction, total</td>
<td>Sertraline &gt; fluvoxamine (Luvox), nefazodone; SSRI &gt; moclobemide</td>
</tr>
<tr>
<td>Sexual satisfaction</td>
<td>Bupropion, nefazodone &gt; sertraline</td>
</tr>
</tbody>
</table>

> = "is associated with a greater incidence of the measured outcome than"; SSRI = selective serotonin reuptake inhibitor.

*--Not available in the United States.

note: No significant difference was found for the following: sertraline vs. citalopram (Celexa); paroxetine (Paxil) vs. fluvoxamine or fluoxetine; amitriptyline vs. amoxapine (Asendin) or mirtazapine (Remeron); clomipramine (Anafranil) vs. fluoxetine, fluvoxamine, paroxetine, sertraline, or citalopram; phenelzine (Nardil) vs. imipramine (Tofranil).

Information from references 1 through 4

There were no other consistent differences between classes of antidepressants. One trial reported less sexual dysfunction resulting from amitriptyline than from sertraline (NNH: seven), but numerous trials have not shown differences between clomipramine (Anafranil) and other SSRIs. One trial showed less sexual dysfunction resulting from fluvoxamine than from sertraline (NNH: six), but no differences between other SSRIs have been demonstrated. Limitations to many of the published studies include small sample sizes, failure to control for baseline differences in sexual function between groups of patients, and lack of uniform means of inquiring into sexual adverse effects.

**Recommendations from Others**

Guidelines issued by the American Psychiatric Association (APA) and the American College of PhysiciansAmerican Society of Internal Medicine (ACPASIM) do not provide specific
recommendations regarding which antidepressant to prescribe to minimize sexual dysfunction. [References 5 and 6—Evidence level 1A] The APA notes that SSRIs can carry a risk of sexual side effects, whereas the ACPASIM states that the data are insufficient to estimate incidence rates, thus making quantitative comparisons among antidepressants impossible.

Clinical Commentary

Bupropion appears to be the best antidepressant for use in patients who are concerned about drug-related sexual dysfunction. Amitriptyline may be a less expensive and suitable alternative, but it has other worrisome adverse effects. Nefazodone may have a low incidence of sexual dysfunction, but it has been associated with hepatotoxicity and was withdrawn from the Canadian and European markets. Moclobemide is not available in the United States.

Clinical Inquiries provide answers to questions submitted by practicing family physicians to the Family Practice Inquiries Network (FPIN). Members of the network select questions based on their relevance to family medicine. Answers are drawn from an approved set of evidence-based resources and undergo peer review. The strength of recommendations and the level of evidence for individual studies are rated using criteria developed by the Evidence-Based Medicine Working Group (http://www.cebm.net/levels_of_evidence.asp).

This series of Clinical Inquiries is coordinated for American Family Physician by John Epling, M.D., State University of New York Upstate Medical University, Syracuse, N.Y. The complete database of evidence-based questions and answers is copyrighted by FPIN.

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REFERENCES


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