Care of the Sexually Active Depressed Patient

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There are several possible causes of sexual dysfunction in depressed patients. A core symptom of depression is anhedonia, including loss of libido. Therefore, determining a cause of sexual dysfunction in a depressed patient can be very difficult, and the differential diagnosis must include a primary sexual dysfunction, sexual dysfunction associated with general medical and psychiatric disorders, and sexual dysfunction associated with treatments for psychiatric disorders. Of particular clinical interest is sexual dysfunction associated with different classes of antidepressant drugs, such as tricyclic antidepressants, selective serotonin reuptake inhibitors, or venlafaxine. Sexual dysfunction's pharmacologic basis is thought to be stimulation of 5-HT_2 receptors. Antidepressant-induced sexual dysfunction, most frequently presenting as a reduction in libido or delayed orgasm, may not pose a large burden for patients in acute treatment. However, in long-term treatment, patients are generally well, and anything that interferes with sexual functioning will be a greater problem and will contribute strongly to noncompliance. Different strategies are advised when dealing with sexual dysfunction in depressed patients treated with antidepressant drugs: waiting for a spontaneous resolution of a problem, reduction in antidepressant drug dosages, drug holidays, adjunctive pharmacotherapy, or switching antidepressants. Perhaps the best way is to avoid sexual dysfunction by starting treatment with an antidepressant with proven acute and long-term efficacy that is devoid of sexual side effects, for example, mirtazapine, bupropion, or nefazodone. *(J Clin Psychiatry 1999;60[suppl 17]:32–35)*

The prevalence of sexual dysfunction in the general population is hard to ascertain since there is a general lack of data. However, an American community study,[1] based on personal interviews with 3432 men and women between the ages of 18 and 59 years, reported that the most common types of sexual dysfunction were low libido (34%) and orgasm disorder in women (24%, mainly delayed orgasm) and premature ejaculation in men (29%). Other types of sexual dysfunction included vaginismus (15% of women), impotence (10% of men), and inhibited orgasm (10% of men). As with the general population, there is also a scarcity of data regarding the prevalence of sexual dysfunction in patients with depression; however, a study of drug-free depressed patients by Mathew and Weinman[2] in 1982 reported a prevalence of 31% for decreased libido in all patients and 35% for erectile dysfunction and 47% for delayed ejaculation in male patients. The corresponding frequency of sexual dysfunction for the control population in this study was 6% for decreased libido, 6% for delayed ejaculation, and no erectile dysfunction. Depressed patients had significantly higher scores for alterations of libido than controls ($p < .04$).

Attitudes about sex in a sample of people taken from the general population (N = 6143) were similar to those in a subpopulation of depressed persons (N = 1140).[3] The percentages of the population for whom having good sex was "fairly" or "very" important were 70% for the general population and 75% for the depressed subpopulation. Loss of sexual interest would prompt 3% of the total population and 2% of the depressed subpopulation to visit the treating physician.

CAUSES OF SEXUAL DYSFUNCTION IN THE DEPRESSED PATIENT

Anhedonia, including loss of libido, is a core symptom of depression, so determining the cause of sexual dysfunction in depressed patients can sometimes be difficult. There are several possible causes of sexual dysfunction in depressed patients, and these can be divided into 3 major groups: nonpsychiatric causes, psychiatric disorders, and psychotropic medications.[4] The main causes of sexual dysfunction in depressed patients include psychiatric or general medical illness, primary sexual dysfunction, and the side effects of medication, psychotropic or otherwise.[5] This article will concentrate on sexual dysfunction resulting from psychotropic medications and the strategies that can be used to alleviate the problem.

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Table 1. Causes of Sexual Dysfunction: Psychotropic Medications for Mood Disorders[a]

Mood stabilizers
Lithium
Carbamazepine
Benzodiazepines
Alprazolam
Diazepam
Clonazepam
Tricyclic antidepressants (TCAs)
Imipramine
Clomipramine
Monoamine oxidase inhibitors
Phenelzine
Selective serotonin reuptake inhibitors (SSRIs)
Fluoxetine
Sertraline
Paroxetine
Fluvoxamine
Citalopram
Other
Venlafaxine

[a]Adapted from reference 5, with permission.

Table 2. Prevalence of Sexual Dysfunction With Antidepressants[a]

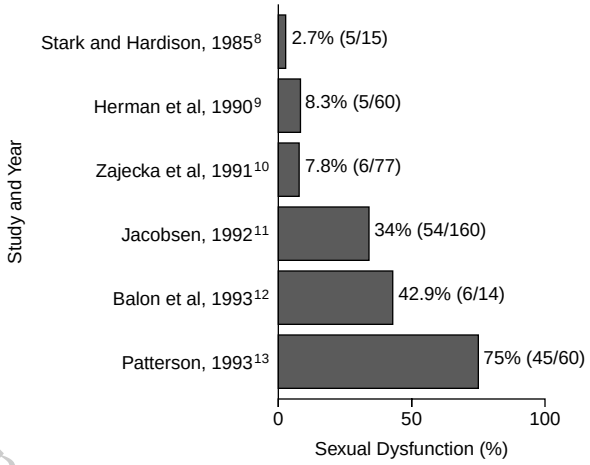
Drug Class	Physicians' Desk Reference[b] %	Clinic[c] %
TCAs	NA	2–95
SSRIs	2–16	4–75
Venlafaxine	2–12	1–12
Bupropion	3	3
Nefazodone	1	< 1
Mirtazapine	< 1	< 1

[a]Abbreviation: NA = no data available.
[b]Data from reference 6.
[c]Data from reference 7.

Table 3. SSRI-Induced Sexual Dysfunction

Libido
Usually decreased, but increases also observed
Excitement
Impotence
Painful erections
Decreased vaginal lubrication
Orgasm
Delayed orgasm
Impaired/painful ejaculation
Anorgasmia in women

Figure 1. Fluoxetine-Induced Sexual Dysfunction[a]



[a]From reference 14, with permission.

A depressed patient may not mind sexual dysfunction arising during acute treatment with antidepressants. However, during long-term treatment, especially if the patient is generally well, prolonged sexual dysfunction constitutes a greater problem and may contribute to poor compliance with drug therapy. There are many psychotropic medications that have been shown to cause sexual dysfunction, particularly those used for mood disorders, and a comprehensive list of these is given in Table 1. The prevalence of sexual dysfunction with the various types of antidepressants is shown in Table 2. Details of the sexual dysfunction encountered with selective serotonin reuptake inhibitors (SSRIs) are given in Table 3.

It is now clear that treatment with SSRIs can be associated with most forms of sexual dysfunction, but the main effects of SSRIs in sexual dysfunction involve sexual excitement and orgasm. The incidence of sexual dysfunction encountered with fluoxetine treatment in various studies over the years is shown in Figure 1.[8–13] It would appear that over recent years, there has been an increase in sexual dysfunction with fluoxetine treatment; however, the reasons for this apparent increase may also be due to the changes in the methods of enquiry (direct questioning versus questionnaires), an increase in clinicians' awareness of the problem, or even a greater willingness of patients to discuss sexual problems.

CARE OF THE DEPRESSED PATIENT WITH SEXUAL DYSFUNCTION

As we have seen, it is important that the assessment of sexual dysfunction is performed correctly. It is essential to obtain a pretreatment (i.e., baseline) level of sexual functioning and to ask patients directly about sexual function. This need was clearly seen in a study of clomipramine by Monterio et al.[15] in which the percentage of patients with sexual dysfunction elicited by questionnaire was 36% and the percentage of patients with serious sexual difficulties elicited by a direct interview was 96%.

There are several strategies for managing antidepressant-induced sexual dysfunction. The most obvious option is to wait for a sufficient period to ensure that the loss of sexual function is not a temporary problem that is unrelated to the antidepressant medication. If there is no change in the situation, then reducing the antidepressant

Table 4. Improved Sexual Functioning During 3-Day Drug Holidays: Patients Taking SSRIs Who Reported "Much" or "Very Much" Improved Sexual Functioning[a]

Measure	Sertraline Group (N = 10)	Paroxetine Group (N = 10)	Fluoxetine Group (N = 10)
Orgasm function, %	60*	50	10
Sexual satisfaction, %	50*	50*	0
Libido, %	50*	50*	0

[a]Data from reference 16.
*p < .05 vs. fluoxetine.

Table 5. Pharmacotherapy for SSRI-Induced Anorgasmia[a]

Drug	Mechanism	Dosage (mg/d)
Cyproheptadine[b]	5-HT antagonist	4–8
Buspirone	5-HT_{1A} partial antagonist	15–45
Yohimbine[b]	Adrenergic antagonist (α_2)	5.4–10.8
Amantadine	Dopamine agonist	100–400
Methylphenidate	Dopamine agonist	10–30
Bupropion	Unknown	75–100
Mirtazapine	5-HT_2 + 5-HT_3 antagonist	15–45

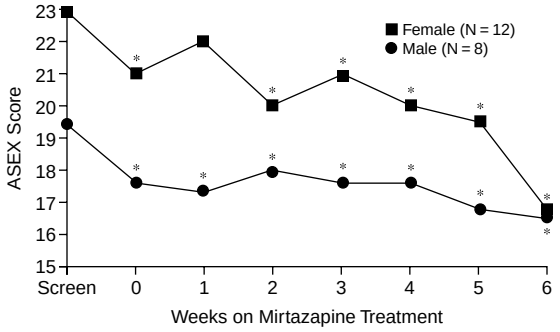
[a]Adapted from reference 5, with permission.
[b]With prn dosing.

dose is the next step. In the event of no amelioration in sexual function after reducing the dosage of antidepressant, a drug holiday in which the drug is withdrawn for a time can often improve sexual function, even after a relatively short drug holiday. The positive results of 3-day drug holidays for patients taking SSRIs are shown in Table 4.[16] In this study, patients taking sertraline and paroxetine reported "much" or "very much" improved sexual function, whereas those taking fluoxetine reported little change. Depression scores did not significantly worsen during the drug holiday.

Adjunctive pharmacotherapy to the offending antidepressant therapy represents another option. The adjunctive pharmacotherapy for SSRI-induced anorgasmia is shown in Table 5 and includes serotonin (5-HT) antagonists and dopamine agonists. Finally, if adjunctive pharmacotherapy does not improve sexual function on existing antidepressant treatment, then it is worth considering switching antidepressants. The results of the change in sexual function after switching from SSRIs to mirtazapine is shown in Figure 2.[17] The improvement in sexual function with mirtazapine compared with SSRIs was significant for both males and females at 6 weeks (p < .01). These results were obtained in an ongoing pilot study currently involving 19 patients who are in remission from major depression with SSRI-related sexual dysfunction. Another study in which patients experiencing sexual dysfunction (orgasm delay or failure) while taking fluoxetine were switched to bupropion showed that there was a complete resolution of orgasm dysfunction in 84% of patients and partial resolution in 10%.[18] Libido was "much" or "very much" improved in 81% of patients.

Of course, ideally, the problem of sexual dysfunction should be avoided by starting patients on therapy with one

Figure 2. Change in Sexual Function After Switch From SSRI to Mirtazapine (LOCF analysis)[a]



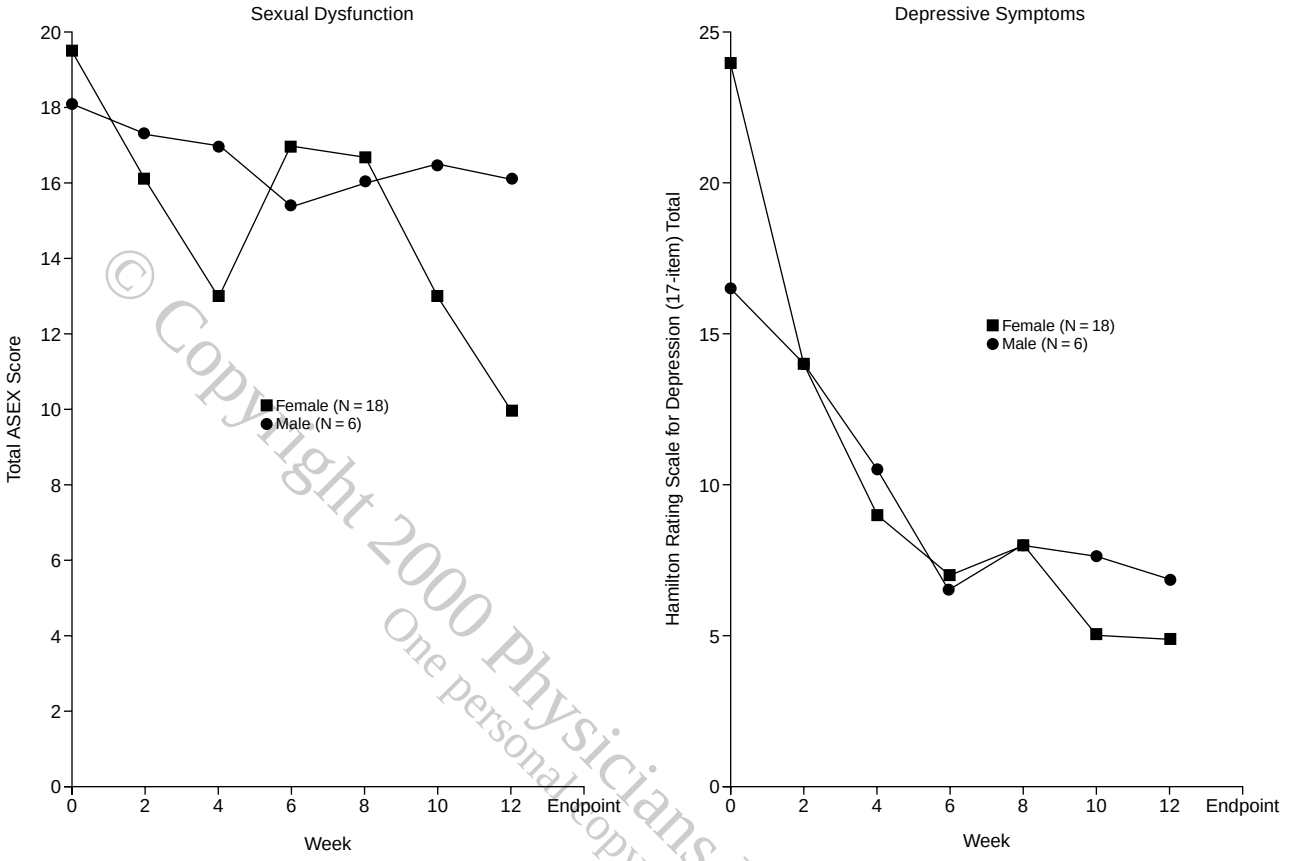
[a]Data from reference 17. Abbreviation: ASEX = Arizona Sexual Experience Scale.
*p < .01.

of the new antidepressants such as nefazodone or mirtazapine, which do not have sexual dysfunction as a side effect. The results of a 6-week, double-blind study[19] of nefazodone versus sertraline in 100 sexually active patients with major depression showed that 49% of men taking sertraline experience difficulty with ejaculation compared with 6% of men taking nefazodone. Similarly, 27% of women taking sertraline experienced difficulty with orgasm compared with 16% of women taking nefazodone.[19] There was a significant difference between the 2 drugs in this study in favor of nefazodone (p < .05). The preliminary results of a current, open-label study[20] of mirtazapine in sexually active outpatients with major depression showed a reduction in both depressive symptoms and sexual dysfunction with mirtazapine (Figure 3). Indeed, this study suggested that sexual function increased during mirtazapine treatment. Measures of desire, arousal, and orgasm were all increased by approximately 33%.[20]

SUMMARY AND CONCLUSIONS

In conclusion, sexual dysfunction is frequent in both the general population and the depressed population, and both of these groups exhibit similarly high levels of concern about sexual dysfunction. Antidepressant-induced sexual dysfunction presents a substantial problem that needs to be addressed, and it is extremely important that physicians specifically inquire whether there are any sexual difficulties by direct interview of the patients. Sexual dysfunction is frequently missed when symptoms are elicited by other means, such as a questionnaire. There are several strategies for dealing with the problem of sexual dysfunction in patients on antidepressants, but perhaps the most useful of all is to avoid the problem from the start of treatment by using an antidepressant, such as mirtazapine, bupropion, or nefazodone, which does not have sexual side effects.

Figure 3. Open-Label Study of Mirtazapine in Sexually Active Outpatients With Major Depression[a]



[a]Data from reference 20.

Drug names: alprazolam (Xanax and others), amantadine (Symmetrel and others), bupropion (Wellbutrin), buspirone (BuSpar), carbamazepine (Tegretol and others), citalopram (Celexa), clomipramine (Anafranil and others), clonazepam (Klonopin and others), cyproheptadine (Periactin), diazepam (Valium and others), fluoxetine (Prozac), fluvoxamine (Luvox), methylphenidate (Ritalin), mirtazapine (Remeron), nefazodone (Serzone), paroxetine (Paxil), phenelzine (Nardil), sertraline (Zoloft), venlafaxine (Effexor), yohimbine (Yocon and others).

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