Antidepressant-Induced Sexual Dysfunction During Treatment With Moclobemide, Paroxetine, Sertraline, and Venlafaxine

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Background: Recent reports suggest that adverse effects on sexual function occur in up to 50% of patients who are treated with selective serotonin reuptake inhibitor (SSRI) antidepressants. Previously cited low rates were more likely a function of underreporting than underoccurrence. There is less evidence about rates of dysfunction with serotonin-norepinephrine reuptake inhibitor (SNRI) and reversible inhibitor of monoamine oxidase A (RIMA) antidepressants. The purpose of this report is to evaluate disturbances in sexual drive/desire and arousal/orgasm in 107 patients who met criteria for major depressive disorder and received treatment with either moclobemide, paroxetine, sertraline, or venlafaxine.

Method: All consenting eligible patients who met DSM-IV criteria for major depressive disorder completed the Sexual Functioning Questionnaire, version 1 (SFQ) and were assessed using the 17-item Hamilton Rating Scale for Depression (HAM-D) prior to and after 8 or 14 weeks of antidepressant therapy. Analyses were carried out to examine the effect of gender, drug type, pretreatment level of sexual dysfunction, and drug response on reported sexual dysfunction.

Results: Compared with women, men experienced a significantly greater level of drug-related impairment in drive/desire ($p < .05$), whereas there were no statistically significant differences in levels of arousal/orgasm impairment between men and women. The reported impairment in drive/desire items for men ranged from 38% to 50% and from 26% to 32% for women. No differences were found across the 4 antidepressants in men, whereas in women, rates of dysfunction were generally higher with sertraline and paroxetine, but only significantly so in comparison with moclobemide on some measures ($p < .03$). Rates of sexual dysfunction with venlafaxine tended to fall between those of SSRIs and the RIMA agent. An unexpected relationship was found between favorable drug response and a decreased level of drug-induced sexual dysfunction.

Conclusion: Antidepressant-induced sexual dysfunction occurs in approximately 30% to 70% of patients who are treated with sertraline or paroxetine. Lower rates are reported with moclobemide and venlafaxine. Clinicians should evaluate the various aspects of sexual dysfunction before and during antidepressant therapy.

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Reports on the frequency of antidepressant-induced sexual dysfunction have been inconsistent and are generally thought to represent an underreporting of such symptoms.[1] This underreporting is largely due to the absence of a systematic approach to data collection. Reports based on direct questioning or specific self-report interviews suggest that up to 50% of depressed patients who are treated with selective serotonin reuptake inhibitors (SSRIs) report some form of sexual dysfunction,[2–7] while other sources, including the *Physicians' Desk Reference*[8] and the *Compendium of Pharmaceuticals and Specialties*,[9] report sexual dysfunction among depressed patients who are treated with sertraline, paroxetine, or fluoxetine as a side effect in fewer than 20% of cases. In contrast to the SSRI agents, nefazodone and bupropion appear to be associated with fewer unwanted sexual side effects.[10–12]

The frequency of sexual dysfunction associated with 2 other antidepressants, venlafaxine, a serotonin and norepinephrine inhibitor, and moclobemide, a reversible inhibitor of monoamine oxidase A (not available in the United States, but available in Canada, Europe, Australia, and other countries), is less well documented. On the basis of a previous report of a favorable sexual side effect profile with moclobemide in healthy volunteers,[13] we hypothesized that moclobemide would have a significantly lower sexual side effect profile than sertraline, paroxetine, or venlafaxine.

Although not the focus of this study, evidence of lack of sexual interest and impairment of sexual function has been reported in drug-free patients with major depression. Baldwin[14] estimated that the rate of sexual dysfunction in

untreated unipolar depressed patients ranged from 35% to 47%, and similar findings were reported from our center, with 40% to 50% of men and women reporting decreased levels of arousal and 15% to 20% reporting ejaculatory or orgasm difficulties before initiating antidepressant therapy.[15]

In this study, we examined the effect of gender, drug type, pretreatment level of sexual dysfunction, and antidepressant response on the reporting of sexual side effects during treatment with 4 antidepressant agents: moclobemide, paroxetine, sertraline, and venlafaxine.

METHOD

Participants

This study was conducted at the Depression Clinic, Centre for Addiction and Mental Health (CAMH), Toronto, Ontario, Canada, and was approved by the Human Scientific and Ethics Review Committee of the CAMH. Subjects were outpatients referred for a psychiatric consultation who gave written informed consent, met criteria for major depressive disorder and were currently experiencing a nonpsychotic major depressive episode according to DSM-IV (with or without other secondary nonpsychotic Axis I disorders), scored a minimum of 16 on the 17-item Hamilton Rating Scale for Depression (HAM-D),[16] were physically healthy with no concurrent active medical illness, and had been free of antidepressant (and other psychotropic) medication for at least 2 weeks (5 weeks for fluoxetine) before the initial study visit. In addition, they were required to have reported sexual activity during the past month.

Measures

The Sexual Functioning Questionnaire, version 1 (SFQ)[15] is a recently constructed self-report questionnaire designed to assess 3 domains of sexual functioning (desire, arousal, and orgasm) modified from Healy[17] (see Appendix 1). Two dimensional subscales were constructed to assess these domains, one scale corresponding to drive and desire (drive/desire) and the other corresponding to arousal and orgasm (arousal/orgasm). The drive/desire scale consists of 4 items and is identical for men and women. The arousal/orgasm scale consists of different sets of items for men and women. For women, this scale contains 3 items, whereas for men, it has 5 items.

Respondents were asked to indicate on a 3-point Likert scale whether each item was experienced less often than usual, the same, or more often than usual in the month preceding assessment. The presence of a dysfunction that was not reported at the time of treatment initiation, or the worsening of a preexisting dysfunction, was scored 1, while the continuation of a preexisting dysfunction or the absence of dysfunction was scored 0. To equate the range of scores for both men and women, proportional scores were calculated. The drive/desire and arousal/orgasm scales were prorated to score 5 points as a maximum level of dysfunction. An additional question was included to assess involvement in sexual activity during the past month.

The SFQ was developed at this site, and although this version of the SFQ was preliminary and has been subsequently revised, its reliability and validity have been established in a previous report on the frequency of sexual dysfunction in drug-free patients who had not yet commenced antidepressant treatment.[15]

Procedure

At the initial study visit (Time 1), the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID)[18] and HAM-D were completed by a trained clinical rater; following this, each patient was asked to complete the SFQ. Also at this visit, clinicians prescribed the most appropriate antidepressant from among the 4 study drugs: moclobemide, paroxetine, sertraline, and venlafaxine. During the study, clinicians provided standard clinical management with clinical visits every 2 weeks, while repeat measures of HAM-D (completed by the same research staff) and SFQ were collected after 8 or 14 weeks of treatment (Time 2).

Statistical Analyses

Mean differences for continuous scores on the SFQ between and among groups were determined using t tests and 1-way analysis of variance, respectively. Chi-square analyses were employed for dichotomously based variables. Regression analyses were used to determine if pretreatment (Time 1) sexual dysfunction was predictive of week 8 or 14 (Time 2) sexual dysfunction.

RESULTS

Patient Characteristics

One hundred seventy-four patients (68 men, 106 women) were entered into the clinical database during the time period for this study. Of these 174 patients, 107 (42 men, 65 women) were treated for at least 8 weeks and completed the SFQ at Time 1 and Time 2. No significant differences were found between patients who completed the study and the patients who did not complete the study (N = 67; 39%) on demographic and clinical variables, including age ($t = 0.60$, $df = 174$, $p = .55$), number of previous episodes ($t = 0.44$, $df = 174$, $p = .66$), and duration of current episode ($t = 0.21$, $df = 174$, $p = .84$).

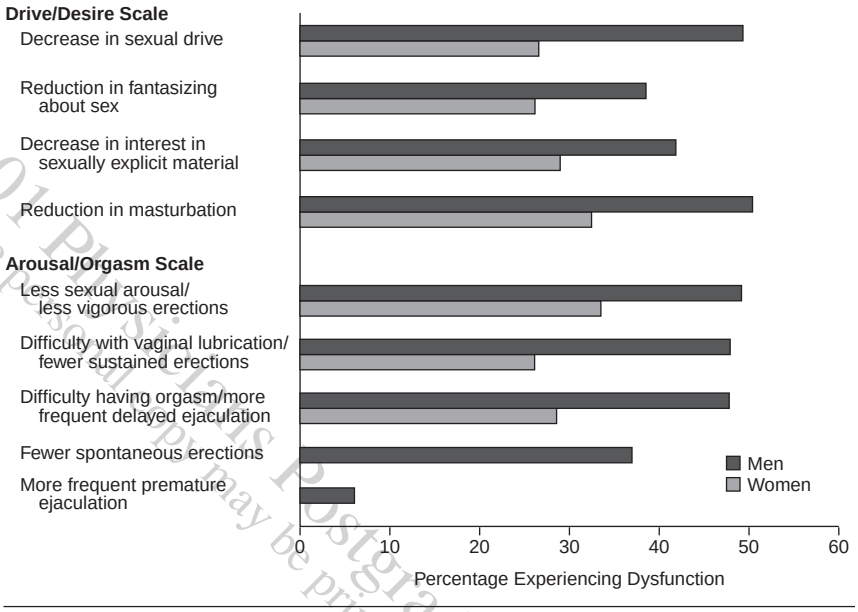
Of the 107 patients who completed the minimum treatment requirement, most (N = 93; 87%) provided Time-2 assessment data at 8 or 14 weeks. Seventeen of these patients received additional prescription medications. Six were taking concomitant hypnotics, 4 were taking oral contraceptives, 3 were taking continuing stable doses of L-thyroxine, 2 were taking β-blocker agents, and 2

were taking nonsteroidal anti-inflammatory agents. These prescription medications were evenly distributed across drug groups. Table 1 displays the demographic and clinical characteristics for each of the 4 antidepressant medication groups. A 1-way analysis of variance indicated that the patients in the different medication groups did not differ with respect to age ($F = 1.49$, $df = 3,104$; $p = .22$), number of previous episodes ($F = 2.15$, $df = 3,104$; $p = .10$), duration of current episodes ($F = 0.94$, $df = 3,104$; $p = .43$), or severity of depression as measured by the HAM-D at Time 1 ($F = 2.8$, $df = 3,103$; $p = .08$).

Table 1. Patient and Drug Characteristics Across Antidepressants

Characteristic	Moclobemide	Sertraline	Paroxetine	Venlafaxine
Subjects				
Men	4	4	20	14
Women	11	22	10	22
Age, y, mean ± SD				
Men	37.4 ± 11.9	38.5 ± 12.6	36.6 ± 9.1	43.7 ± 12.3
Women	36.5 ± 8.5	37.7 ± 12.6	36.9 ± 12.1	40.5 ± 10.3
Mean ± SD dose, mg/d	485.0 ± 278.9	99.0 ± 51.3	30.7 ± 13.9	151.6 ± 80.7
Dose range, mg/d	150–900	50–200	10–80	37.5–375
No. of prior episodes, mean ± SD	1.7 ± 1.0	2.0 ± 1.3	2.6 ± 1.5	2.8 ± 1.6
Duration of current episode, wk, mean ± SD	79.5 ± 83.8	64.5 ± 75.8	45.0 ± 43.9	68.2 ± 57.9

Figure 1. Antidepressant-Induced Sexual Dysfunction



Gender Differences

The first set of analyses addressed gender differences in sexual dysfunction. The percentages of men and women who reported new or added dysfunction for each individual item from the drive/desire and arousal/orgasm scales during antidepressant treatment are shown in Figure 1. Using the dimensional scale scores, men reported significantly greater drug-induced impairment of drive/desire compared with women (mean ± SD = 2.26 ± 2.02 vs. 1.43 ± 2.12; $t = 6.23$, $df = 107$, $p < .05$). Differences between men and women on the arousal/orgasm scale were not significant (mean ± SD = 1.82 ± 1.51 vs. 1.32 ± 2.0; $t = 1.26$, $df = 107$, $p = .21$).

Antidepressant Medication Differences

The second set of analyses addressed differences in sexual dysfunction across the different antidepressant medications. No significant differences were found in the percentage of men reporting antidepressant-induced sexual dysfunction for the 4 items of the drive/desire scale across the 4 drugs ($\chi^2 = 4.97$, $df = 3$, $p > .17$; Table 2). This was also the case for the 5 items of the arousal/orgasm scale ($\chi^2 = 5.40$, $df = 1$, $p > .14$).

For women, based on a 2 (dysfunction, no dysfunction) × 4 (moclobemide, paroxetine, sertraline, venlafaxine) chi-square analysis, there were no statistically significant differences in antidepressant-induced sexual dysfunction across the 4 drugs. However, examination of Table 3 indicates generally less sexual dysfunction on the drive/desire items for moclobemide and venlafaxine compared with the SSRIs (sertraline and paroxetine). A 2 (dysfunction, no dysfunction) × 2 (venlafaxine, SSRIs) chi-square analysis comparing venlafaxine with the 2 SSRIs revealed no significant differences across the 4 drive/desire items, ($\chi^2 = 2.08$, $df = 1$, $p > .15$). In contrast, a 2 (dysfunction, no dysfunction) × 2 (moclobemide, SSRIs) chi-square analysis comparing the 2 SSRIs with moclobemide indicated more sexual dysfunction with the SSRIs; however, only the masturbation item reached statistical significance ($\chi^2 = 5.03$, $df = 1$, $p < .03$). A subsequent 2 (dysfunction, no dysfunction) × 2 (venlafaxine, moclobemide) chi-square analysis indicated no difference in sexual dysfunction related to drive/desire items between venlafaxine and moclobemide ($\chi^2 = 1.60$, $df = 1$, $p > .21$).

On the arousal/orgasm scale, women again showed lower rates of dysfunction with venlafaxine and moclobemide (see Table 3). However, a 2 (dysfunction, no dysfunction) × 4 (moclobemide, paroxetine, sertraline, venla-

Table 2. Percentage of Men Experiencing Antidepressant-Induced Sexual Dysfunction[a]

	Moclobemide		Sertraline		Paroxetine		Venlafaxine	
SFQ Item	N	%	N	%	N	%	N	%
Drive/desire items								
Decrease in sexual drive	1	25	1	33	10	50	8	57
Reduction in fantasizing about sex	0	0	2	50	7	35	7	50
Decrease in interest in sexually explicit material	2	50	2	50	6	32	7	50
Reduction in masturbation	1	33	2	67	10	53	6	46
Arousal/orgasm items								
Less vigorous erections	2	50	2	50	8	42	8	57
Fewer sustained erections	2	50	3	75	6	30	9	64
Fewer spontaneous erections	2	50	2	50	5	25	6	46
More frequent premature ejaculation	1	25	0	0	1	7	0	0
More frequent delayed ejaculation	1	33	1	25	11	58	5	42

[a]Abbreviation: SFQ = Sexual Functioning Questionnaire, version 1.

Table 3. Percentage of Women Experiencing Antidepressant-Induced Sexual Dysfunction

	Moclobemide		Sertraline		Paroxetine		Venlafaxine	
SFQ Item	N	%	N	%	N	%	N	%
Drive/desire items								
Decrease in sexual drive	1	9	7	32	4	40	5	23
Reduction in fantasizing about sex	2	18	7	33	4	44	3	14
Decrease in interest in sexually explicit material	2	18	8	38	4	40	4	19
Reduction in masturbation	1	9	8	44	4	44	5	28
Arousal/orgasm items								
Less sexual arousal	2	18	10	48	4	40	5	24
Difficulty obtaining vaginal lubrication	1	9	8	40	3	30	4	19
Difficulty achieving orgasm	0	0	7	39	4	57	4	21

Table 4. Comparative Efficacy Across Antidepressants[a]

Measure	Moclobemide (N = 15)	Sertraline (N = 26)	Paroxetine (N = 30)	Venlafaxine (N = 36)
HAM-D score, mean ± SD				
Time 1	20.1 ± 3.9	22.8 ± 3.5	22.4 ± 3.9	21.2 ± 3.6
Time 2	12.0 ± 6.5	10.3 ± 7.3	9.7 ± 7.7	12.0 ± 7.9
Responders, %[b]	33	42	47	39

[a]Abbreviation: HAM-D = Hamilton Rating Scale for Depression.
[b]Response was defined as a reduction of 50% and a score of 7 or less on the HAM-D.

faxine) chi-square analysis of the 3 arousal/orgasm items indicated that only the item assessing "difficulty achieving orgasm" reached statistical significance ($\chi^2 = 9.98$, df = 3, $p < .02$). Furthermore, a 2 (dysfunction, no dysfunction) × 2 (moclobemide, SSRIs) chi-square analysis comparing moclobemide with the SSRIs indicated proportionately significantly less impairment in difficulty achieving orgasm for moclobemide ($\chi^2 = 8.51$, df = 1, $p < .004$). Subsequent analyses on the effect of venlafaxine on sexual dysfunction revealed a statistical trend for venlafaxine to induce proportionately less difficulty with having orgasm compared with paroxetine ($\chi^2 = 2.98$, df = 1, $p < .08$); however, it also revealed a statistical trend for venlafaxine to induce proportionately greater difficulty with having orgasm compared with moclobemide ($\chi^2 = 3.41$, df = 1, $p < .06$).

Baseline Levels of Sexual Dysfunction

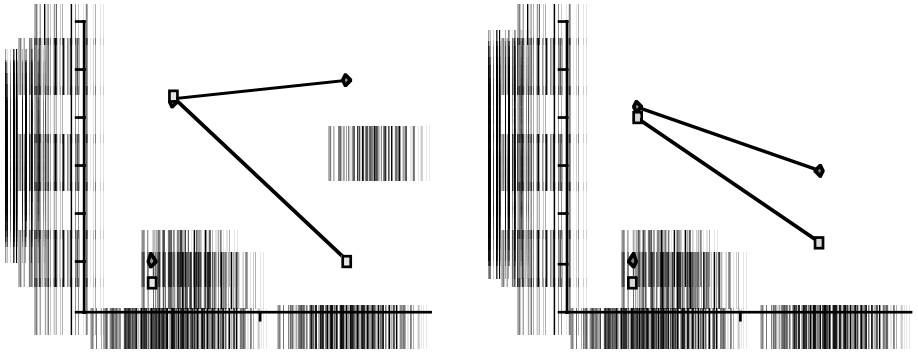
The third set of analyses addressed the effect of pretreatment dysfunction on subsequent reports of drug-induced sexual impairment. It should first be noted that baseline sexual dysfunction did not differ significantly across drugs for men on either the drive/desire ($F = 1.72$, df = 3,32; $p = .18$) or arousal/orgasm ($F = 2.09$, df = 3,35; $p = .12$) scales. The same was true for women on both drive/desire ($F = 2.53$, df = 3,46; $p = .07$) and arousal/orgasm ($F = 1.72$, df = 3,45; $p = .18$). A regression analysis was conducted to determine whether Time-2 sexual dysfunction scores (antidepressant-induced) could be predicted from Time-1 sexual dysfunction scores (depression-induced). Baseline levels of sexual dysfunction were not predictive of Time-2 sexual dysfunction as assessed by the drive/desire scale ($R^2 = 0.003$, $F = 0.31$, df = 1,103; $p = .58$) or the arousal/orgasm scale ($R^2 = 0.02$, $F = 1.06$, df = 1,106; $p = .31$). Thus, baseline sexual functioning did not influence subsequent reports of antidepressant-induced sexual dysfunction.

Drug Response and Sexual Dysfunction

The fourth set of analyses addressed the relationship between drug response and reported antidepressant-induced sexual dysfunction. We first sought to determine if equivalency of response existed across the different antidepressant medication groups. To this end, we performed a repeated-measures analysis of variance, with HAM-D scores serving as the dependent variable. The repeated (within-group) independent variable was time (Time 1 and Time 2) and the between-groups independent variable was antidepressant medication group. There was a significant main effect for time ($F = 206.51$, df = 1,106; $p < .001$), but no group-by-time interaction effect ($F = 2.18$, df = 3,104; $p = .10$), suggesting that all antidepressant medication groups were equally effective in reducing depressive symptoms (Table 4). Using the criteria recommended by Frank and colleagues,[19] we next categorized the patients into responders (i.e., 50% reduction from baseline and a HAM-D item score of 7 or less) and nonresponders and performed a 2 (responder, nonresponder) × 4 (antidepressant medication group) chi-square analysis.

Parallel to the results from the repeated analysis of variance, we found no significant difference in treatment response across the antidepressant medication groups ($\chi^2 = 8.51$, df = 3, p = .84). A comparison of mean doses for each of the 4 antidepressants in responder and nonresponder categories revealed statistically significant differences for women receiving paroxetine (t = 2.97, df = 7, p < .03): female nonresponders were receiving a significantly higher mean daily dose of paroxetine than female responders (30 mg vs. 17.5 mg). All other comparisons were not statistically significant, although the mean daily dose of moclobemide prescribed to female nonresponders was at a clinically significantly higher level compared with responders (570 mg vs. 300 mg).

Figure 2. Relationship Between Response and Antidepressant-Induced Sexual Dysfunction



Since there were no significant treatment effects across drugs, we combined all antidepressant medication groups and then conducted a 2 (men, women) × 2 (response, nonresponse) analysis of variance separately for the drive/desire and arousal/orgasm scales. It should be noted that there were no significant differences between responders and nonresponders on pretreatment levels of sexual dysfunction for either of the scales, for men or women (p > .2 for all). The analysis of variance showed a significant main effect for response in both the drive/desire (F = 6.12, df = 3,89; p < .02) and the arousal/orgasm scales (F = 8.06, df = 3,83; p < .01). Nonresponders reported greater sexual dysfunction following treatment compared with responders. There was a significant sex-by-response interaction for the drive/desire scale (F = 5.02, df = 1,92; p < .03). Whereas women who were nonresponders showed significantly more sexual dysfunction related to drive and desire compared with women who were responders (t = 3.51, df = 54, p < .001), no such differences emerged between male responders and nonresponders (t = 0.27, df = 35, p = .70). No significant interaction effect was found on the arousal/orgasm scale (F = 0.69, df = 1,83; p = .41), indicating that the difference between responders and nonresponders occurred in both men and women (Figure 2).

DISCUSSION

It was hypothesized that decreased sexual interest, arousal, and orgasmic function would occur more frequently in depressed patients who received treatment with sertraline, paroxetine, or venlafaxine compared with moclobemide. These differences were significant between moclobemide and SSRIs, with venlafaxine occupying an intermediate position.

A higher frequency of antidepressant-induced sexual dysfunction occurred in men compared with women. Similarly, in a comparison of sexual dysfunction across 4 SSRI antidepressants, Montejo-Gonzalez and colleagues[20] reported sexual dysfunction in 62% of men and 52% of women, although women reported greater severity. Kavoussi and colleagues[11] reported orgasm dysfunction in 61% of men compared with 41% of women who were treated with sertraline.

The frequency of drive/desire and arousal/orgasm dysfunction associated with sertraline and paroxetine in this study was generally between 30% to 50%. Although different methodologies limit direct comparisons, Modell and associates[12] reported similar rates of SSRI-induced dysfunction; 55% of their depressed patients reported decreased libido; 50%, reduced arousal; and 42%, a reduction in intensity of orgasm. Those authors found that differences in response frequencies among paroxetine, sertraline, and fluoxetine were not significant.[12] Paroxetine, perhaps because of its high potency for serotonin reuptake inhibition, has been noted to have greater sexual side effects,[21] although this finding was not substantiated in an across-SSRI comparison.[22]

Evidence to support a lower rate of sexual dysfunction associated with moclobemide has also been reported in 2 previous studies.[20,23] Twelve of 15 patients with SSRI-induced sexual dysfunction who were switched to moclobemide experienced total improvement.[20] Similarly, Philipp et al.,[23] in a comparative study of moclobemide and doxepin, reported significantly higher rates of improved sexual function in the moclobemide group.

Although there is a paucity of literature on venlafaxine-related sexual dysfunction, the potential benefit of noradrenergic activity, particularly at higher doses, may partially mitigate against serotonergically induced sexual side effects. Support for this benefit comes from preclinical evi-

dence that enhancing central noradrenergic tone increases sexual behavior[24] and from spontaneous patient report data.[25]

This series of depressed patients who received treatment at a university-based clinic reflects natural practice conditions and provides additional comparative information about the incidence of antidepressant-induced sexual dysfunction during the first 8 to 14 weeks of antidepressant therapy. Findings of differences in the frequency of antidepressant-induced sexual dysfunction between men and women, across drugs, and in severity between responders compared with nonresponders require replication with larger samples of patients and with different evaluation scales.

Drug names: bupropion (Wellbutrin), doxepin (Sinequan and others), fluoxetine (Prozac), nefazodone (Serzone), paroxetine (Paxil), sertraline (Zoloft), venlafaxine (Effexor).

REFERENCES

1. Balon R, Yeragani VK, Pohl R, et al. Sexual dysfunction during antidepressant treatment. J Clin Psychiatry 1993;54:209–212
2. Demyttenaere K, De Fruyt J, Sienaert P. Psychotropics and sexuality. Int Clin Psychopharmacol 1998;13(suppl 6):S35–S41
3. Dorevitch A, Davis H. Fluvoxamine associated sexual dysfunction. Ann Pharmacother 1994;28:872–874
4. Segraves RT. Overview of sexual dysfunction complicating the treatment of depression. J Clin Psychiatry Monograph 1992;10(2):4–10
5. Gitlin MJ. Effects of depression and antidepressants on sexual functioning. Bull Menninger Clin 1995;59:233–248
6. Margolese HC, Assalian P. Sexual side effects of antidepressants: a review. J Sex Marital Ther 1996;22:209–217
7. Segraves RT. Antidepressant-induced sexual dysfunction. J Clin Psychiatry 1998;59(suppl 4):48–54
8. Physicians' Desk Reference. Montvale, NJ: Medical Economics; 1995
9. Compendium of Pharmaceuticals and Specialties. 34th ed. Toronto, Ontario: Canadian Pharmaceutical Association; 1999
10. Feiger A, Kiev A, Shrivastava RK, et al. Nefazodone versus sertraline in outpatients with major depression: focus on efficacy, tolerability, and effects on sexual functioning and satisfaction. J Clin Psychiatry 1996;57 (suppl 2):53–62
11. Kavoussi RJ, Segraves RT, Hughes AR, et al. Double-blind comparison of bupropion sustained release and sertraline in depressed outpatients. J Clin Psychiatry 1997;58:532–537
12. Modell JG, Katholi CR, Modell JD, et al. (1997). Pharmacoepidemiology and drug utilization: comparative sexual side effects of bupropion, fluoxetine, paroxetine and sertraline. Clin Pharmacol Ther 1997;61:476–487
13. Kennedy SH, Ralevski E, Davis C, et al. The effects of moclobemide on sexual desire and function in healthy volunteers. Eur Neuropsychopharmacol 1996;6:177–181
14. Baldwin DS. Depression and sexual function. J Psychopharmacol 1996; 10:30–34
15. Kennedy SH, Dickens S, Eisfeld BS, et al. Sexual dysfunction before antidepressant therapy in major depression. J Affect Disord 1999;56:197–204
16. Hamilton M. A rating scale for depression. J Neurol Neurosurg Psychiatry 1960;23:56–62
17. Healy D. Psychiatric Drugs Explained. 2nd ed. London, England: Mosby; 1997
18. First MB, Spitzer RL, Gibbon M, et al. Structured Clinical Interview for DSM-IV Axis I Disorders, Patient Edition (SCID-I/P, Version 2.0). New York, NY: Biometric Research, New York State Psychiatric Institute; 1995
19. Frank E, Prien RF, Jarrett RB, et al. Conceptualization and rationale for consensus definitions of terms in major depressive disorder: remission, recovery, relapse, and recurrence. Arch Gen Psychiatry 1991;48:851–855
20. Montejo-Gonzalez AL, Liorca G, Izquierdo JA, et al. SSRI-induced sexual dysfunction: fluoxetine, paroxetine, sertraline and fluvoxamine in a prospective multicenter and descriptive clinical study of 344 patients. J Sex Marital Ther 1997;23:176–194
21. Lane RM. A critical review of selective serotonin reuptake inhibitor-related sexual dysfunction: incidence, possible aetiology and implications for management. J Psychopharmacol 1997;11:72–82
22. Waldinger MD, Hengeveld MW, Zwinderman AH, et al. The effects of SSRI antidepressants on ejaculation: a double-blind, randomised, placebo-controlled study with fluoxetine, fluvoxamine, paroxetine and sertraline. J Clin Psychopharmacol 1998;18:274–281
23. Philipp M, Kohnen R, Benkert O. A comparison study of moclobemide and doxepin in major depression with special reference to effects on sexual dysfunction. Int Clin Psychopharmacol 1993;7:149–153
24. Bitran D, Hull EM. Pharmacological analysis of male rat sexual behavior. Neurosci Biobehav Rev 1987;11:365–389
25. Schweizer E, Feighner J, Mandos LA, et al. Comparison of venlafaxine and imipramine in the acute treatment of major depression in outpatients. J Clin Psychiatry 1994;55:104–108

Appendix 1: Sexual Functioning Questionnaire Items[a]

Drive/desire items for both men and women
Decrease in sexual drive
Reduction in fantasizing about sex
Decrease in interest in sexually explicit material
Reduction in masturbation
Arousal/orgasm items for men
Less vigorous erections
Fewer sustained erections
Fewer spontaneous erections
More frequent premature ejaculation
More frequent delayed ejaculation
Arousal/orgasm items for women
Less sexual arousal
Difficulty obtaining vaginal lubrication
Difficulty achieving orgasm
Assessment of sexual activity for both men and women
Have you been involved in sexual activity, with or without a partner, within the last month?

[a]From Kennedy et al.[15]