Sexual dysfunction caused by selective serotonin reuptake inhibitors (SSRIs): Management

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INTRODUCTION

Selective serotonin reuptake inhibitors (SSRIs) are first line antidepressants for multiple psychiatric disorders. However, these drugs can interfere with different aspects of sexual functioning, including desire, arousal, and orgasm [1,2]. SSRI-induced sexual dysfunction occurs in both males and females, and can lead to nonadherence.

The frequency of sexual side effects may vary among the different SSRIs. Although it is not known how SSRIs impair sexual functioning, the symptoms appear to be dose dependent [3] and genetic polymorphisms may be involved [4].

Sexual side effects can occur with other classes of antidepressants, including serotonin-norepinephrine reuptake inhibitors, tricyclic antidepressants, and monoamine oxidase inhibitors; however, there are more studies of sexual dysfunction secondary to SSRIs [1,2]. Unipolar major depression can also impair sexual functioning, and treatment with an SSRI can improve satisfaction [3].

This topic reviews the management of sexual dysfunction caused by SSRIs. The pharmacology, administration, and other side effects of SSRIs are discussed separately. (See "Selective serotonin reuptake inhibitors: Pharmacology, administration, and side effects".)

INCIDENCE OF SEXUAL DYSFUNCTION

Studies of sexual problems secondary to SSRIs often underestimate the problem due to methodologic problems, including absence of baseline assessments and comparison groups, and different definitions of sexual dysfunction [2,3].

Sexual dysfunction is one of the most common adverse effects of SSRIs [5]. Although the incidence of SSRI-induced sexual dysfunction in different studies ranges widely from approximately 15 to 80 percent [1,3,6,7], the best estimate is that sexual impairment occurs in roughly 50 percent of patients treated with SSRIs:

- A 14-week, prospective observational study (Sequenced Treatment Alternatives to Relieve Depression [STAR*D]) of 1473 patients treated with citalopram found that [4]:
  - Decreased libido occurred in 54 percent
  - Difficulty achieving orgasm occurred in 36 percent
  - Among the 574 males, erectile dysfunction occurred in 37 percent
- A cross-sectional survey of 704 patients who had started SSRIs or serotonin-norepinephrine reuptake inhibitors estimated that treatment-emergent sexual dysfunction occurred in approximately 50 percent [8].

SSRI-related sexual dysfunction is observed more often in females because they are treated with SSRIs more frequently than males (in a ratio of 2:1) [4].

Although there are rare, anecdotal reports of adverse sexual effects persisting for months or years after discontinuation of SSRI use, there is no compelling evidence that SSRI-induced sexual side effects persist after discontinuation. Based upon our clinical experience, sexual side effects induced by SSRIs resolve soon after the medication is stopped.

ASSESSMENT

SSRIs may worsen pre-existing impairment or cause new onset of dysfunction. We thus suggest that clinicians ask about sexual functioning prior to administering these drugs.

When SSRIs are prescribed, assessment of sexual dysfunction includes questions about different aspects of sexual activity:

- Desire (libido)

- Frequency of sexual activity
- Arousal (lubrication in females and erectile function in males)
- Orgasm (delayed orgasm and anorgasmia)

The assessment should also determine the severity of sexual dysfunction, including the number of impairments and intensity of each.

Several validated screening or severity questionnaires are available for assessing SSRI-induced sexual dysfunction, including The Arizona Sexual Experience Scale and Changes in Sexual Functioning Questionnaire [3,9], as well as the International Index of Erectile Dysfunction (see "Evaluation of male sexual dysfunction", section on 'Validated instruments'). However, these instruments are not part of standard clinical practice and are generally reserved for research settings.

Additional information about evaluating patients with sexual dysfunction is discussed separately. (See "Overview of sexual dysfunction in females: Epidemiology, risk factors, and evaluation" and "Evaluation of male sexual dysfunction".)

MANAGEMENT

General approach — We suggest that management of sexual dysfunction caused by SSRIs proceed according to the sequence described in the algorithm (algorithm 1) and the sections below. Patients first receive initial treatment and progress through each subsequent step until they respond [3]:

- Initial treatment
  - Watchful waiting; if sexual impairment persists:
  - Decrease the dose of the SSRI within the therapeutic range.
- Treatment-resistant patients – Management is determined by the severity of depression and sexual dysfunction:
  - Ongoing depression – For patients who respond only partially to an SSRI (eg, reduction of baseline symptoms <50 percent) or not at all, we suggest switching to a different antidepressant.
  - Improved depression but severe sexual dysfunction – For patients who obtain at least moderate relief of depressive symptoms with an SSRI (eg, reduction of baseline

symptoms ≥50 percent), but suffer severe sexual dysfunction, we suggest switching antidepressants.

- Improved depression and mild to moderate sexual dysfunction – For patients who obtain at least moderate relief of depressive symptoms with an SSRI and whose sexual dysfunction is mild to moderate, we suggest augmenting the SSRI with a second drug.

Each treatment step is described in greater detail in the sections below.

Most treatment strategies and specific treatments have not been compared in head-to-head trials. In addition, the results of some studies are difficult to interpret because it is not clear whether sexual dysfunction began during SSRI treatment and thus represents an adverse effect, or began prior to onset of treatment with SSRIs and represents a symptom of the depressive syndrome or a primary sexual disorder.

Initial treatment of sexual dysfunction — For depressed patients who receive an SSRI and develop sexual dysfunction, we suggest initially waiting (eg, two to eight weeks) for spontaneous remission of the adverse effect (algorithm 1). If sexual impairment persists, we then decrease the dose within the therapeutic range. Although not well studied, these interventions are frequently the first approach taken by many clinicians and experts [3,9].

For SSRI-induced sexual dysfunction, it appears that watchful waiting alone is typically not effective [5]. A prospective observational study in 156 patients treated with fluoxetine, fluvoxamine, paroxetine, or sertraline found that after waiting four to six months, moderate to complete improvement occurred in only 19 percent [10]. Waiting for patients to adapt to the SSRI may work best for patients with mild sexual dysfunction [11].

By contrast, decreasing the dose for patients with SSRI-induced sexual impairment often appears to be helpful. In a prospective observational study (n = 30 patients) in which the dose was decreased by 50 percent, at least moderate improvement occurred in 77 percent [10]. Reducing the dose may be most feasible for remitted patients whose depression has remained stable for at least several weeks or months [3], and for patients taking relatively high doses (eg, escitalopram 30 mg/day or paroxetine 50 mg/day) or suffering additional adverse effects.

However, decreasing the dose may diminish therapeutic effects; thus, the dose should be decreased slowly in small increments and should not be reduced below the minimum therapeutic dose [3]. In addition, patients should be monitored. As an example, sertraline 200 mg per day can be reduced by 25 to 50 mg per day every two to four weeks, with patients interviewed prior to each decrease. The minimum therapeutic dose for sertraline is typically 50

mg per day (table 1). (See "Selective serotonin reuptake inhibitors: Pharmacology, administration, and side effects", section on 'Dose'.)

Treatment-resistant sexual dysfunction

Overview — Sexual dysfunction caused by SSRIs often does not respond to either watchful waiting or lower doses [12]. Treatment options for these patients include switching to a different antidepressant, or augmenting the SSRI with a second drug. The choice depends upon the degree of relief from the depressive syndrome and the degree of sexual impairment (algorithm 1):

- Ongoing depression – For patients who respond only partially to the SSRI (eg, reduction of baseline depressive symptoms <50 percent) or not at all, we suggest switching to a different antidepressant.
- Improved depression but severe sexual dysfunction – For patients who obtain at least moderate relief of depressive symptoms with an SSRI (eg, reduction of baseline symptoms ≥50 percent) but suffer severe sexual dysfunction (eg, impairment occurs almost always during sexual activity), we suggest switching to a different antidepressant.
- Improved depression and mild to moderate sexual dysfunction – For patients who obtain at least moderate relief of depressive symptoms with an SSRI and whose sexual dysfunction is mild to moderate (eg, impairment occurs half the time during sexual activity), we suggest augmenting the SSRI with a second drug:
  - Males
    - For males with erectile dysfunction, we suggest adjunctive treatment with a phosphodiesterase-5 inhibitor.
  - Females
    - For females with low libido, we typically suggest add-on bupropion at relatively high doses within the therapeutic range (eg, bupropion extended release 300 mg/day).
    - For females with delayed orgasm or anorgasmia, we suggest a phosphodiesterase-5 inhibitor.

  However, a reasonable alternative for both males and females is to switch antidepressants.

Switching antidepressants is often preferable to augmentation because adherence may be better with monotherapy than combination treatment [13]. In addition, monotherapy may cause fewer adverse effects, cost less, and present fewer risks of drug interactions in patients taking medications for other conditions. Conversely, augmentation with a second drug maintains the benefit derived from the SSRI, whereas switching antidepressants may lead to relapse of depression or new adverse effects [11]. No head-to-head trials have compared switching with augmentation.

General information about implementing a switch from one antidepressant to another is discussed separately. (See "Switching antidepressant medications in adults", section on 'Switching antidepressant medications'.)

Ongoing depression — Some patients with SSRI-induced sexual dysfunction may also have ongoing depression, such that they respond only partially to the SSRI (eg, reduction of baseline depressive symptoms <50 percent), or not at all. For these patients, we suggest switching to a non-SSRI antidepressant (eg, bupropion), based upon studies that indicate several antidepressants cause fewer adverse sexual effects than SSRIs (table 2) [1,6,14]. However, a reasonable alternative is to switch to a different SSRI. No head-to-head trials have compared these strategies.

Multiple options are available for patients who decide to switch antidepressants. In selecting a new drug, the choice is based upon factors such as past treatment history, availability, potential side effects, cost, and patient preference. The different options, listed in order of preference, are as follows:

- **Bupropion** – Several randomized trials have demonstrated that bupropion does not impair sexual functioning and that sexual dysfunction occurs less often with bupropion than SSRIs [15]:

  - A meta-analysis of patient level data from five randomized trials, lasting 6 to 16 weeks, compared bupropion sustained release, SSRIs (fluoxetine or sertraline), and placebo in 1228 patients with unipolar major depression who did not meet criteria for sexual desire disorder [16]. Treatment-emergent sexual desire disorder occurred in fewer patients who received bupropion than SSRIs (6 versus 17 percent) and was identical with bupropion and placebo (6 percent). The incidence of sexual arousal disorder and orgasmic dysfunction were also less with bupropion than SSRIs, and comparable for bupropion and placebo.

  - A meta-analysis of patient level data from two randomized trials, each lasting eight weeks, compared bupropion extended release (300 or 450 mg per day), escitalopram

(10 or 20 mg per day), and placebo in 830 patients with unipolar major depression and normal sexual functioning [17]. Worsened sexual functioning occurred in fewer patients who received bupropion than escitalopram (20 versus 36 percent), and was comparable with bupropion and placebo (20 and 15 percent).

- A network meta-analysis of 37 randomized trials (n >14,000 depressed patients) found that sexual dysfunction occurred less often with bupropion than escitalopram, paroxetine, or sertraline [7].

In addition, observational studies suggest that switching from an SSRI to bupropion can be beneficial. One prospective study in 31 patients with fluoxetine-induced sexual dysfunction found that after switching from fluoxetine to bupropion, sexual functioning was much or very much improved in 81 percent [18].

Indirect evidence that suggests switching to bupropion may ameliorate SSRI-induced sexual dysfunction includes a randomized trial that found add-on bupropion can treat sexual function induced by SSRIs [19]. In addition, bupropion can treat females with low libido (sexual interest/arousal disorder) that is not induced by SSRIs. (See "Overview of sexual dysfunction in females: Management", section on 'Bupropion'.)

The pharmacology, administration, and side effects of bupropion are discussed separately. (See "Atypical antidepressants: Pharmacology, administration, and side effects", section on 'Bupropion'.)

- **Other non-SSRIs** – Sexual dysfunction that emerges during treatment with SSRIs may persist despite switching to bupropion. For these patients, we suggest discontinuing bupropion and switching to mirtazapine [5,20]. Evidence supporting the use of mirtazapine includes a meta-analysis of four randomized trials (n = 907 patients with major depression) that compared mirtazapine with SSRIs (fluoxetine, paroxetine, or sertraline), and found that sexual dysfunction was less likely with mirtazapine (odds ratio 0.3, 95% CI 0.1-0.7) [21]. The pharmacology, administration, and side effects of mirtazapine are discussed separately. (See "Atypical antidepressants: Pharmacology, administration, and side effects", section on 'Mirtazapine'.)

  However, reasonable alternatives to mirtazapine include agomelatine (not available in the United States), moclobemide (not available in the United States), and selegiline. A pooled analysis of randomized trials and prospective and retrospective observational studies found that sexual impairment was comparable for agomelatine, moclobemide, selegiline, and placebo [1]. Extra caution is required if patients are switched directly from SSRIs to

monoamine oxidase inhibitors such as moclobemide or selegiline. (See "Switching antidepressant medications in adults", section on 'Switching to or from MAOIs'.)

Another reasonable alternative to mirtazapine is vortioxetine. In one trial, investigators enrolled patients (n = 447) who responded to citalopram, paroxetine, or sertraline for unipolar major depression, but also developed sexual dysfunction as a side effect [22]. Patients were randomly assigned to switch to vortioxetine (10 or 20 mg/day) or escitalopram (10 or 20 mg/day) for eight weeks. Improvement of sexual dysfunction was greater with vortioxetine than escitalopram, and antidepressant efficacy was maintained with each drug. Discontinuation of treatment due to adverse effects with vortioxetine occurred in 9 percent of patients and with escitalopram in 6 percent.

When switching from SSRIs to non-SSRIs to relieve sexual dysfunction, another option is nefazodone [7]. In one study that enrolled male and female patients with sexual impairment due to sertraline, the drug was discontinued for two weeks [23]. Patients whose sexual dysfunction resolved (n = 72) were then randomly assigned to nefazodone (400 mg per day) or sertraline (100 mg per day) for eight weeks; reemergence of sexual dysfunction occurred in fewer patients treated with nefazodone than sertraline (26 versus 76 percent). However, some clinicians avoid nefazodone because of concerns about hepatic toxicity. (See "Serotonin modulators: Pharmacology, administration, and side effects", section on 'Side effects'.)

- **Different SSRI** – Switching to a different SSRI (eg, fluoxetine) may ameliorate sexual impairment and appeal to patients who otherwise were satisfied with the initial SSRI. However, the degree of sexual dysfunction may be so substantial that patients insist upon switching to a non-SSRI. In addition, few head-to-head studies have compared sexual dysfunction among different SSRIs.

  Low quality data suggest that the incidence of sexual dysfunction may possibly be greater with escitalopram or paroxetine than fluoxetine and other second-generation antidepressants, but the evidence is considered weak [15]. A network meta-analysis of 37 randomized trials (n >14,000 depressed patients) evaluated the adverse effects of 13 second-generation antidepressants by using results from direct comparisons between the drugs, as well as indirectly comparing drugs through their relative effect with a common comparator (typically placebo) [7]. The incidence of sexual dysfunction was greater with escitalopram than fluoxetine, mirtazapine, and nefazodone, and dysfunction was also greater with paroxetine than fluoxetine, mirtazapine, nefazodone, and venlafaxine. However, the credible intervals were wide; this, along with the indirect comparisons, led

the investigators to conclude that they could not precisely estimate the comparative risk of sexual impairment associated with specific antidepressants.

Information about implementing a switch from an SSRI to bupropion, another non-SSRI antidepressant, or a different SSRI is discussed separately. (See "Switching antidepressant medications in adults".)

Improved depression but severe sexual dysfunction — For depressed patients who obtain at least moderate relief with an SSRI (eg, reduction of baseline depressive symptoms ≥50 percent), but suffer severe sexual dysfunction (eg, impairment occurs almost always during sexual activity), we suggest switching antidepressants. Multiple options are available for patients who decide to switch antidepressants. In selecting a new drug, the choice is based upon factors such as past treatment history, availability, potential side effects, cost, and patient preference. The specific antidepressants that we use for switching are described in the section immediately above and are listed in order of preference. (See 'Ongoing depression' above.)

Improved depression and mild to moderate sexual dysfunction — For patients who obtain at least moderate relief of depressive symptoms with an SSRI (eg, reduction of baseline depressive symptoms ≥50 percent), and whose sexual dysfunction is mild to moderate (eg, impairment occurs half the time during sexual activity), we suggest augmenting the SSRI with a second drug. However, a reasonable alternative to augmentation is to switch antidepressants; choosing a new antidepressant is described elsewhere in this topic. (See 'Ongoing depression' above.)

Choosing add-on pharmacotherapy for SSRI-induced sexual dysfunction depends upon the patient's sex:

Males — For males with SSRI-induced sexual dysfunction, we recommend adjunctive treatment with a phosphodiesterase-5 inhibitor, based upon multiple randomized trials:

- A meta-analysis of two trials compared adjunctive sildenafil (50 or 100 mg before sexual activity) with placebo for six or eight weeks in 112 euthymic males with sexual dysfunction caused by ongoing antidepressant treatment (primarily SSRIs), and found that improvement of rating scale scores was greater with sildenafil [2].

  The larger of the two trials included 89 patients with remitted unipolar major depression who were continuing to receive antidepressants (largely SSRIs) and were experiencing sexual dysfunction, including low libido (64 percent), erectile dysfunction (87 percent), delayed ejaculation (70 percent), and anorgasmia (21 percent) [24]. Overall (global) sexual dysfunction was much improved or very much improved in more patients who received

sildenafil than placebo (55 versus 4 percent). In addition, sexual desire (libido), erectile function, and orgasm function each improved more with sildenafil than placebo. However, headache occurred in four times as many patients who received sildenafil than placebo (40 and 10 percent), flushing occurred in eight times as many patients who received sildenafil (17 and 2 percent), transient visual disturbances in twice as many patients with sildenafil (12 and 5 percent), and nasal congestion in six times as many patients with sildenafil (12 and 2 percent). None of the patients suffered a relapse of major depression.

- A pooled analysis of 19 trials (lasting 12 weeks) compared tadalafil with placebo in males with erectile dysfunction [25]. In the subgroup (n = 205) who were taking antidepressants (SSRIs or other types), successful intercourse occurred in more patients treated with tadalafil 10 or 20 mg per day, compared with patients who received placebo (54 and 59 versus 29 percent). This finding was consistent with the demonstrated efficacy of tadalafil for the general treatment of erectile dysfunction. In addition, tadalafil was well tolerated in the subgroup taking antidepressants.

- A subsequent 12-week randomized trial compared tadalafil (20 mg taken on demand) with placebo in 50 males with SSRI-induced sexual impairment who completed the study (out of 54 enrolled) [26]. Erections and sexual activity improved in more males who received tadalafil than placebo (92 versus 8 percent). In addition, improvement of each domain of sexual functioning (desire, erectile function, orgasm, intercourse satisfaction, and overall satisfaction) was greater with tadalafil than placebo, and active treatment was well tolerated.

It is highly likely that other phosphodiesterase-5 inhibitors (eg, avanafil and vardenafil) are beneficial for males with SSRI-induced sexual dysfunction.

Specific interactions between an SSRI and a phosphodiesterase-5 inhibitor may be determined using the Lexicomp drug interactions tool (Lexi-Interact Online) included in UpToDate. Information about phosphodiesterase-5 inhibitors is discussed separately in the context of treating sexual dysfunction the general population of males. (See "Treatment of male sexual dysfunction", section on 'Initial therapy: PDE5 inhibitors'.)

Females — For females with SSRI-induced sexual dysfunction, add-on pharmacotherapy depends upon the specific sexual impairment:

- **Low libido** – For females with SSRI-induced low libido (sexual interest/arousal disorder), we suggest augmentation with bupropion at relatively high doses within the therapeutic range (eg, 300 mg/day). A four-week randomized trial compared add-on bupropion (sustained release 150 mg twice daily) with placebo in 42 patients who had remitted from

unipolar major depression, were continuing to receive an SSRI, and were suffering sexual dysfunction, including low libido; 37 (88 percent) of the patients were females [19]. Improvement of desire and frequency of sexual activity was greater with add-on bupropion. However, irritability occurred nearly three times as often with bupropion than placebo (60 and 23 percent of patients). (A meta-analysis of three trials [n = 482 patients] also found that adjunctive bupropion sustained release (150 mg twice per day) improved sexual dysfunction [2], but the largest trial [n = 227] was retracted [27]).

Two other small, randomized trials found that a relatively low dose of adjunctive bupropion (sustained release 150 mg once daily) was not efficacious for SSRI-induced sexual dysfunction, including libido [28,29]. The pharmacology, administration, and side effects of bupropion are discussed separately. (See "Atypical antidepressants: Pharmacology, administration, and side effects", section on 'Bupropion'.)

Several reasonable alternatives to bupropion are available to manage low sexual interest caused by SSRIs. These alternatives include nonpharmacologic interventions as well as medications such as bremelanotide; however, these approaches were studied in the general population of females with low sexual interest, rather than patients with SSRI-related low sexual interest. (See "Overview of sexual dysfunction in females: Management".)

- **Orgasmic disorder** – For females with SSRI-induced orgasmic disorder, we suggest pharmacotherapy or nonpharmacologic interventions, depending upon availability and patient preference. Nonpharmacologic approaches are discussed separately. (See "Treatment of female orgasmic disorder", section on 'Psychosocial interventions' and "Overview of sexual dysfunction in females: Management", section on 'Orgasmic disorder'.)

  For females who prefer pharmacotherapy, we suggest a phosphodiesterase-5 inhibitor, based upon one randomized trial. An eight-week trial compared sildenafil (50 or 100 mg before sexual activity) with placebo in females (n = 98) with remitted major depression and sexual dysfunction due to ongoing antidepressants (primarily SSRIs) [30]. Overall improvement of sexual dysfunction occurred in more patients who received sildenafil than placebo (72 versus 27 percent). However, the benefit of sildenafil was limited to delayed orgasm and anorgasmia; the drug provided no advantage for sexual desire or arousal (eg, lubrication). In addition, dyspepsia, flushing, nasal congestion, and visual disturbance each occurred more frequently with sildenafil, and 43 percent of the sildenafil patients reported headaches. Using a phosphodiesterase-5 inhibitor for female orgasmic disorder is suggested only for females with SSRI-induced orgasmic disorder, rather than the

general population of females with orgasmic disorder. (See "Treatment of female orgasmic disorder", section on 'Medication'.)

Specific interactions between an SSRI and another drug such as bupropion or a phosphodiesterase-5 inhibitor may be determined using the Lexicomp drug interactions tool (Lexi-Interact Online) included in UpToDate.

Treatments with little to no demonstrated benefit — For sexual side effects caused by SSRIs, we do not suggest augmentation with amantadine, bethanechol, buspirone, cyproheptadine, ephedrine, ginkgo biloba, granisetron, mirtazapine, olanzapine, or yohimbine; a systematic review of randomized trials found no benefit with these adjunctive drugs [2]. Similarly, we do not suggest add-on treatment with stimulants such as dextroamphetamine, methylphenidate, and pemoline; although they have been used adjunctively for SSRI-induced sexual dysfunction [9], support for their effectiveness is limited to case reports [11].

In addition, we do not suggest add-on treatment with flibanserin for females who are taking SSRIs and have low libido. There are no published data regarding the use of flibanserin for antidepressant induced low libido, and the benefits of flibanserin for hypoactive sexual desire disorder are modest. (See "Overview of sexual dysfunction in females: Management", section on 'Flibanserin'.)

Other options that have been attempted for sexual dysfunction caused by SSRIs include the following, but the evidence supporting their use is poor:

- **Exercise** – A randomized trial compared exercise (30 minutes of moderate strength training and cardiovascular exercise, three times/week) immediately before sexual activity with exercise separate from sexual activity in 52 females who reported antidepressant sexual side effects; nearly half were treated with SSRIs [31]. After three weeks, patients crossed over to the other intervention. Sexual desire and overall sexual function improved more with exercise immediately prior to sexual activity. However, many of the females were not distressed by the antidepressant sexual side effects, and the study was marked by a high rate of attrition (46 percent).

- **Drug holiday** – Although drug holidays (briefly interrupting treatment) may possibly be useful for sexual dysfunction induced by SSRIs other than fluoxetine, which has a relatively long half-life, this approach is not widely used [9]. One observational study of weekend drug holidays found that in patients taking paroxetine (n = 10) or sertraline (n = 10), libido, orgasm, and sexual satisfaction improved in half of the patients; however, no benefit occurred in patients taking fluoxetine (n = 10) [32]. Potential problems with drug holidays include the risk of worsening depression and discontinuation syndromes [3], as well as

sending the wrong message about adherence (especially during maintenance treatment) [33].

SOCIETY GUIDELINE LINKS

Links to society and government-sponsored guidelines from selected countries and regions around the world are provided separately. (See "Society guideline links: Depressive disorders".)

INFORMATION FOR PATIENTS

UpToDate offers two types of patient education materials, “The Basics” and “Beyond the Basics.” The Basics patient education pieces are written in plain language, at the 5th to 6th grade reading level, and they answer the four or five key questions a patient might have about a given condition. These articles are best for patients who want a general overview and who prefer short, easy-to-read materials. Beyond the Basics patient education pieces are longer, more sophisticated, and more detailed. These articles are written at the 10th to 12th grade reading level and are best for patients who want in-depth information and are comfortable with some medical jargon.

Here are the patient education articles that are relevant to this topic. We encourage you to print or e-mail these topics to your patients. (You can also locate patient education articles on a variety of subjects by searching on “patient info” and the keyword(s) of interest.)

- Beyond the Basics topics (see "Patient education: Sexual problems in men (Beyond the Basics)" and "Patient education: Sexual problems in females (Beyond the Basics)")

SUMMARY AND RECOMMENDATIONS

- **Manifestation and incidence of sexual dysfunction** – Selective serotonin reuptake inhibitors (SSRIs) can cause sexual dysfunction in males and females, including decreased libido, decreased arousal, and delayed orgasm and anorgasmia. Among patients receiving SSRIs, the estimated incidence of sexual dysfunction is roughly 50 percent. (See 'Introduction' above and 'Incidence of sexual dysfunction' above.)

- **Assessment** – Assessment of sexual dysfunction secondary to SSRIs includes questions about desire, frequency of sexual activity, arousal, and orgasm. (See 'Assessment' above

and "Overview of sexual dysfunction in females: Epidemiology, risk factors, and evaluation" and "Evaluation of male sexual dysfunction".)

- **Initial management** – Our initial approach for patients with SSRI-induced sexual dysfunction is to wait (eg, two to eight weeks) for spontaneous remission of the sexual impairment; if the impairment persists, we decrease the dose within the therapeutic dose range (algorithm 1). (See 'Initial treatment of sexual dysfunction' above.)

- **Treatment-resistant sexual dysfunction** – Patients with SSRI-induced sexual dysfunction often do not respond to watchful waiting or lower doses. Management of treatment-resistant sexual dysfunction depends upon the efficacy of the SSRI in treating the depressive syndrome and the severity of sexual dysfunction:

  - **Ongoing depression** – For patients whose depression responds only partially to an SSRI (eg, reduction of baseline depressive symptoms <50 percent) or not at all, we suggest switching antidepressants, rather than augmenting the SSRI with a second drug (**Grade 2C**). This approach addresses both the depressive syndrome and the sexual dysfunction. We typically switch to bupropion; however, reasonable alternatives include mirtazapine, agomelatine, moclobemide, selegiline, and vortioxetine, as well as a different SSRI. (See 'Ongoing depression' above.)

  - **Improved depression but severe sexual dysfunction** – For patients who obtain at least moderate relief of depressive symptoms with an SSRI (eg, reduction of baseline symptoms ≥50 percent) but suffer severe sexual dysfunction (eg, impairment occurs almost always during sexual activity), we suggest switching antidepressants, rather than augmenting the SSRI with a second drug (**Grade 2C**). This approach addresses both the depressive syndrome and the sexual dysfunction. We typically switch to bupropion. (See 'Improved depression but severe sexual dysfunction' above.)

  - **Improved depression and mild to moderate sexual dysfunction** – For patients who obtain at least moderate relief of depressive symptoms with an SSRI and whose sexual dysfunction is mild to moderate (eg, impairment occurs half the time during sexual activity), we suggest augmenting the SSRI with a second drug to manage the sexual dysfunction:

    - **Males** – We use add-on treatment with a phosphodiesterase-5 inhibitor for males, similar to the general population of males with sexual dysfunction. (See 'Males' above and "Treatment of male sexual dysfunction", section on 'Initial therapy: PDE5 inhibitors'.)

- **Females** – For females with low libido, we suggest add-on bupropion at relatively high doses within the therapeutic range, rather than other drugs (**Grade 2C**). For females with delayed orgasm or anorgasmia, we suggest add-on treatment with a phosphodiesterase-5 inhibitor rather than other drugs (**Grade 2C**). (See 'Females' above.)

However, a reasonable alternative to augmentation for both males and females is switching antidepressants. (See 'Improved depression and mild to moderate sexual dysfunction' above.)

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