Pharmacologic Treatment of Body Dysmorphic Disorder: Review of the Evidence and a Recommended Treatment Approach

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ABSTRACT

Research on effective pharmacotherapy for body dysmorphic disorder (BDD) has rapidly increased in recent years, with emerging data consistently indicating that serotonin reuptake inhibitors (SRIs) are often efficacious for this disorder. Although data are limited, it appears that higher SRI doses and longer treatment trials than those used for many other psychiatric disorders are often needed to treat BDD effectively. Approaches to treatment-resistant BDD have received little investigation, but available data indicate that switching to another SRI and several SRI-augmentation strategies may be helpful. This article reviews the empirical literature on BDD and offers a recommended approach to the pharmacotherapy of this distressing and often disabling disorder.

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INTRODUCTION

The pharmacotherapy of body dysmorphic disorder (BDD) involves several apparent paradoxes. One paradox is that although the empirical literature on this disorder's pharmacologic treatment is limited, there appears to be considerable consensus on how clinicians should initially treat these patients.[1] Perhaps a more fundamental paradox involves the very nature of the disorder: BDD is a disorder of disturbed body image, which almost certainly has sociological, cultural, and psychological roots,[2] yet many patients respond to medication.

As recently as the 1980s, patients with BDD were described as "extremely difficult" to treat,[3] and a noted dermatologist stated, "The author knows of no more difficult patients to treat than those with body dysmorphic disorder."[4] However, as emerging empirical evidence and clinical experience indicate that most patients with BDD may benefit from pharmacotherapy, this pessimism is gradually being replaced by a measured optimism.

It should first be underscored that BDD warrants aggressive treatment. Patients with this disorder are markedly distressed, with scores on measures of perceived stress exceeding those reported for most psychiatric patients.[5] Most patients experience significant impairment in social and occupational/academic functioning.[6-8] Many are housebound, require psychiatric hospitalization, and attempt suicide.[6-8] Quality of life is notably poor: one study found that mental health-related quality of life for BDD patients was poorer than for the United States' population as a whole as well as for patients with depression or a chronic or acute medical condition (eg, diabetes or acute myocardial infarction).[9] Furthermore, although it is relatively common,[10] BDD usually goes undiagnosed in clinical settings.[11,12]

WHY TREAT BODY-IMAGE DISTURBANCE WITH MEDICATION?

There are a number of reasons to think that medication might be effective for BDD. Obsessional preoccupation with perceived appearance flaws and compulsive, repetitive behaviors, such as mirror-checking, excessive grooming, and skin-picking, are core features of the disorder.[6] In some ways, BDD resembles obsessive-compulsive disorder (OCD)[13] and this suggests a role for serotonin reuptake inhibitors (SRIs). Many patients have notable depressive features,[6,14] suggesting a role for antidepressants. Insight is usually poor or absent, and nearly half of patients are delusional[7] (ie, completely convinced that their view of their appearance "defect" is accurate), raising the question of whether antipsychotics may be useful. In addition, although the development of BDD almost certainly involves psychological and sociocultural factors, it also likely involves neurobiological disturbances,[2] with very preliminary data suggesting a role for abnormalities in serotonergic function[15,16] and corticostriatal circuitry.[17] Moreover, other types of body-image disturbance, such as autotopagnosia (disorientation with respect to body surface) or unilateral neglect (involving a decreased awareness of body parts) are well known to have a neurologic basis. While these disturbances do not have direct implications for pharmacotherapy, they highlight the neurobiologic basis of some types of body-image abnormalities.[18]

Although most patients with BDD seek often-costly nonpsychiatric treatment, such as dermatologic treatment and cosmetic surgery,[19] available data indicate that these

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approaches are usually ineffective. In a study of 250 adults with BDD seen in a psychiatric setting, who received a total of 484 nonpsychiatric treatments, only 7.3% of all treatments led to both a decrease in concern with the treated body part and overall improvement in BDD.[19] Although prospective data are lacking, these findings suggest that nonpsychiatric treatment should not be recommended for these patients. Reports of BDD patients being violent toward surgeons[20] or committing suicide in a dermatology setting[21,22] underscore the importance of implementing more effective treatment for BDD.

EVIDENCE ON THE EFFICACY OF MEDICATION FOR BDD

Serotonin Reuptake Inhibitors

The SRIs (clomipramine and the selective SRIs [SSRIs]) have received the lion's share of pharmacologic research. Data from clinical series, open-label studies, and controlled studies consistently indicate that these agents are often, and perhaps selectively, effective as single agents for BDD. SRIs are widely used and recommended for BDD.[1] Response to an SRI usually results in decreased distress and time preoccupied with the "defect," improved functioning (eg, return to work or school), and improvement in depressive symptoms.[23] Repetitive behaviors, such as mirror-checking and skin-picking, usually improve.[23]

Case Reports

Several early case reports suggested efficacy for fluoxetine and clomipramine,[24-26] in some cases after failure to respond to a variety of psychotropic agents. Efficacy of SSRIs in children and adolescents was subsequently reported,[27-30] with relapses occurring after medication discontinuation.[27] Intravenous, pulse-loaded clomipramine was also noted to be efficacious in two cases.[31]

Retrospective Studies

Largely retrospective data from larger patient series suggest that SRIs, but not other medications, are often effective for BDD. In an early series of 30 patients, 58% responded to SRIs, whereas only 5% responded to other medications.[6] In an expansion of this series, consisting of 130 patients who had received a total of 316 medication trials, 42% of 65 SRI trials led to improvement on the Clinical Global Impressions (CGI) scale, compared to 30% of 23 trials with monoamine oxidase inhibitors (MAOIs), 15% of 48 trials with non-SRI tricyclics, 3% with neuroleptics, 6% with a variety of other medications (eg, benzodiazepines and mood stabilizers), and 0% of electroconvulsive therapy (ECT) trials.[32] (Although in this series the SRI response rate was higher than for the other medications, it was relatively low compared with subsequent rates reported later in this article. This probably reflects the fact that at this early stage of BDD research, it was not known what an adequate SRI trial consisted of, and many patients received SRI doses and trial durations that were probably inadequate for treating BDD). Another retrospective study of 50 patients by Hollander and colleagues[33] similarly reported that 35 SRI trials resulted in improvement in BDD symptoms, whereas 18 non-SRI tricyclic trials led to no overall improvement in BDD symptoms.

Prospective Clinical Series

In a recent chart-review study of 90 patients treated by the author in her clinical practice, clinically significant improvement occurred with 63.2% (n=55) of adequate SRI trials, with similar response rates for each type of SRI.[34] In this study, 17.5% (n=10) of adequate SRI trials resulted in full remission and 31.7% (n=18) in partial remission.[34]

In a study of 33 children and adolescents with BDD,[35] 10 of 19 (53%) subjects treated with an SRI had an improvement in BDD symptoms on the CGI, and 10 (45%) of 22 SRI trials led to an improvement. Considering only the 13 SRI trials conducted by the authors, which tended to be more aggressive trials, eight (62%) resulted in improvement in BDD. No non-SRI medications (n=8 trials) were effective for BDD.

Open-Label Studies

Three systematic open-label studies of SRIs have been done, two with fluvoxamine and one with citalopram. In a 16-week study of 30 subjects who met criteria for the *Diagnostic and Statistical Manual of Mental Disorders*, Fourth Edition, (*DSM-IV*) BDD,[23] 19 (63%) patients responded (in an intent-to-treat analysis) based on ≥30% improvement on the Yale-Brown Obsessive-Compulsive Scale Modified for BDD (BDD-YBOCS)[36] and the CGI. BDD-YBOCS scores significantly decreased, from 31.1±5.4 at baseline to 16.9±11.8 at termination. Six responders discontinued fluvoxamine, all of whom relapsed, with BDD symptoms significantly improving in the four patients who restarted an SRI. In a 10-week open-label study of fluvoxamine up to 300 mg/day,[37] 10 of 15 patients were much or very much improved on the CGI. Ten of 12 patients who completed the study were responders. In a recent open-label study of citalopram in 15 BDD patients, BDD-YBOCS scores decreased from 30.7±4.9 at baseline to 15.3±10.6 at termination ($P<.001$), with 73.3% (n=11) of subjects rated as responders on the BDD-YBOCS and the CGI (KA Phillips, MD, and F Najjar MD, unpublished data, 2001).

Controlled Studies

Two controlled-treatment trials of BDD have been completed. In the first, a double-blind crossover study of clomipramine versus desipramine conducted by Hollander and colleagues,[38] subjects were treated for 8 weeks with each medication. Forty patients entered the study and 29 were randomized. Clomipramine was superior to desipramine in improving BDD symptoms and functional disability. Treatment efficacy was independent of the presence or severity of comorbid diagnoses of OCD, depression, or social phobia. This study is important because, consistent with the aforementioned retrospective data, it suggests that BDD should be treated with an SRI rather than a non-SRI antidepressant.

The first placebo-controlled study was recently completed. It found that fluoxetine was more effective than placebo for BDD.[39] Seventy-four patients with *DSM-IV* BDD

criteria were enrolled and 67 were randomized to 12 weeks of treatment in this double-blind, parallel-group study. Fluoxetine was significantly more effective than placebo for BDD beginning at week 8 and continuing at weeks 10 and 12 (<.001). The response rate was 53% (18 of 34) to fluoxetine and 18% (6 of 33) to placebo (P=.003). As in the clomipramine/desipramine study, treatment efficacy was independent of the presence of major depression or OCD.

Efficacy of SRIs for Delusional BDD

Perhaps the most intriguing finding in the pharmacotherapy literature is that patients with delusional BDD appear to respond to SRIs.[7,34,35,38-40] This finding is counterintuitive, given that these patients are diagnosed not only with BDD but also with a psychotic disorder (delusional disorder of the somatic type), a group of disorders usually treated with antipsychotics. In the previously noted placebo-controlled fluoxetine study, a similar percentage of delusional and nondelusional patients had response of BDD symptoms to fluoxetine (50% and 55%, respectively).[39] In the desipramine/clomipramine crossover study, clomipramine was more effective than desipramine regardless of whether patients had insight or held their dysmorphic misperception with delusional intensity.[38] Of interest, clomipramine was even more effective for delusional patients than for nondelusional patients. The results from these controlled studies are consistent with earlier findings from case reports,[24,25,29] clinical series,[7,35] and open-label trials,[40] which also indicated that delusional patients had a high rate of response to SRIs. Several of these studies[39,40] had the methodologic advantage of using a reliable and valid scale[41] to classify subjects prior to treatment as delusional or nondelusional.

Several studies also examined the different question of whether insight improves with treatment. In other words, do treated patients develop more accurate beliefs about their appearance, realizing that they do not look abnormal? In an open-label fluvoxamine study, insight significantly improved.[40] In the blinded crossover study, clomipramine but not desipramine resulted in significant improvement in insight.[38] In the fluoxetine study, insight did not improve more with fluoxetine than with placebo, although insight improved significantly more in treatment responders (to either fluoxetine or placebo) than in treatment nonresponders.[39]

These intriguing findings indicate that SRIs are effective for BDD symptoms in delusional patients. They also suggest that insight may improve with SRI treatment, although the data are somewhat contradictory. These data further suggest that certain types of psychosis (perhaps the delusional variants of putative OCD-spectrum disorders) may respond to SRIs alone.

Other Antidepressants

Venlafaxine, a mixed serotonin-norepinephrine reuptake inhibitor, may have a role in treating BDD. Although there are no published reports on this medication's efficacy, in the author's clinical experience, BDD may respond to venlafaxine, even after the failure of numerous SRIs. More systematic research on this medication's efficacy is clearly warranted. MAOIs, too, may have a role in treating BDD. In the author's aforementioned retrospective series, MAOIs were effective in 30% of 23 cases, in some cases after patients failed an SRI.[7] Several case reports have noted a good response to MAOIs, one with tranylcypromine and one with a combination of phenelzine, trimipramine, and perphenazine.[42]

Tricyclic antidepressants other than clomipramine appear generally ineffective for BDD. The clomipramine/desipramine trial described above found that desipramine was significantly less effective than clomipramine for BDD.[38] Because the study did not include a placebo control, it cannot be stated with certainty that desipramine is ineffective for BDD (it is possible that placebo would have produced an even lower response rate). However, other published data are consistent with a comparative lack of efficacy for tricyclics other than clomipramine. A previously noted retrospective study of 50 patients found that non-SRI tricyclic trials led to no overall improvement in BDD symptoms,[33] and the author's previously noted retrospective series found that only 15% of 48 trials with non-SRI tricyclics improved BDD symptoms.[32]

There are no data available on the efficacy of mirtazapine and bupropion for BDD, and only very limited data on nefazodone.[34] In the author's experience, these medications are generally ineffective as single agents for BDD.

Antipsychotics as Single Agents

Given that a high percentage of patients with BDD are delusional, an important question is whether antipsychotics are effective as single agents for BDD, including its delusional form. This question has received surprisingly little empirical investigation. In early case reports, antipsychotics were generally reported to be ineffective, with negative results for loxitane, trifluoperazine, thioridazine, fluphenthixol, pimozide, and unspecified agents.[42] The author's previously noted retrospectively assessed series, in which 52% of patients had been delusional, showed a response in only 1 of 49 trials.[7] A recent case report, however, noted improvement in BDD symptoms with olanzapine.[43]

Pimozide has had the reputation of being effective for monosymptomatic hypochondriacal psychosis, a broad category currently known as delusional disorder of the somatic type, which includes delusional BDD.[3] However, data from only a small number of case reports are available for patients clearly diagnosed with delusional BDD as opposed to another type of somatic delusional disorder. These reports suggest that pimozide may be effective for BDD, although the author has found pimozide alone to be ineffective in a small number of cases (n=8).[32] The efficacy of this medication warrants further, more rigorous investigation.

Other Medications as Single Agents

Data are very limited but generally suggest that other medications are generally ineffective as single agents for BDD (although they may have a role as SRI-augmentation

agents, as discussed in a later section). Early case reports noted a lack of response for lithium, alprazolam, diazepam, and unspecified benzodiazepines.[42] The author's previously noted retrospective study similarly found that a variety of other medications (eg, mood stabilizers, benzodiazepines, stimulants), used alone, were usually ineffective for BDD.[32] In the previously described series of 33 children and adolescents with BDD,[35] none of the eight treatments with non-SRI medications significantly decreased BDD symptoms.

OTHER SOMATIC TREATMENTS

Electroconvulsive Therapy

There are only limited data on the efficacy of ECT. A 1991 review found seven published case reports, six of which reported an unsuccessful outcome with ECT.[42] One subsequent report noted a good response to ECT.[44] In the author's series of 130 cases, none of eight ECT trials was successful, although the data were largely retrospective.[32] The author is aware of approximately 10 additional cases, none of which showed ECT efficacy for BDD, although several patients had a transient improvement, primarily in depressive symptoms.

Psychosurgery

One published case report noted improvement in BDD symptoms with a modified leucotomy.[45] In another, significant improvement occurred with a capsulotomy (P Mindus, MD, oral communication, 2001), and in a third case, with a bilateral anterior cingulotomy and subcaudate tractotomy (E Cassem, MD, personal communication, 2001). However, in two cases, an anterior capsulotomy was ineffective for BDD (SA Rasmussen, oral communication, 2001).

SEROTONIN REUPTAKE INHIBITOR AUGMENTATION STRATEGIES

SRI augmentation with pharmacotherapy has considerable face validity. Augmentation strategies are widely used in other disorders, including OCD and depression, disorders with similiarites to BDD. Augmentation has a particular

TABLE. SUMMARY OF CONTROLLED AND OPEN-LABEL PHARMACOTHERAPY STUDIES IN BDD*

Medication	Study design	N	Trial duration and mean dose (mg/day)	Results†	Reference
Fluoxetine	Randomized, double-blind, placebo-controlled, parallel group trial	74 entered; 67 randomized	12 weeks 77.7±8.0 (range=40–80)	Fluoxetine was significantly more effective than placebo (response rate of 53% vs 18% on BDD-YBOCS‡); effect size: *d*=0.70	39
Clomipramine vs desipramine	Randomized, double-blind, crossover trial	40 entered; 29 randomized	16 weeks (8 weeks on each drug) CMI: 138±87 DMI: 147±80	Clomipramine was significantly more effective than desipramine for BDD symptoms and functional disability (response rate of 65% vs 35% on BDD-YBOCS§)	38
Fluvoxamine	Open-label trial	30	16 weeks 238.3±85.8 (range=50–300)	63% of subjects responded to fluvoxamine on BDD-YBOCS‡	23
Fluvoxamine	Open-label trial	15	10 weeks 208.3±63.4 (range=100–300)	10 subjects responded to fluvoxamine on the CGI	37
Citalopram	Open-label trial	15	12 weeks 51.3±16.9 (range=10–60)	73% of subjects responded to citalopram on BDD-YBOCS‡; quality of life and functioning also significantly improved	\\

BDD-YBOCS=the Yale-Brown Obsessive-Compulsive Scale Modified for Body Dysmorphic Disorder; CMI=clomipramine; DMI=desipramine; CGI=Clinical Global Impressions scale.

*Case reports, case series, and retrospective studies are not included in the table but are described in the text.

†Results are reported for an intent-to-treat analysis for all studies except for the clomipramine/desipramine trial, which used a minimum treatment analysis.

‡Response was defined as 30% or greater decrease in total BDD-YBOCS score; the BDD-YBOCS assesses BDD severity during the past week based on preoccupation with the perceived defect (time occupied, interference with functioning due to the preoccupation, distress, resistance, and control), associated repetitive behaviors, such as mirror-checking (time spent, interference with functioning, distress if the behaviors are prevented, resistance, and control), insight, and avoidance.

§Response was defined as ≥25% decrease in total BDD-YBOCS score.

\\ KA Phillips KA,MD, and F Najjar, MD, unpublished data, 2001.

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appeal for patients who have partially responded to an SRI and for whom relapse—which could occur with a switch to another SRI—could be risky (eg, leading to increased suicide risk). SRI-augmentation strategies may in fact be more effective for patients who have had a partial SRI response, as opposed to no SRI response, with a chart-review study reporting augmentation response rates of 40.5% (n=15) for partial SRI responders versus only 18.2% for SRI nonresponders (P=.04).[34]

Buspirone

A rationale for using buspirone is that it is a partial agonist at 5-HT_{1A} receptors, and it has been shown to effectively augment SRIs in depression[46] and in some studies of OCD.[47] In a chart-review study of BDD patients in which buspirone was added to an SRI after an adequate trial, 33.3% (n=12) of trials were successful, with a large effect size.[34] The mean buspirone dose was 56.5±15.2 mg/day. Buspirone augmentation of SRIs appears as effective for delusional as nondelusional patients.[48]

Clomipramine Plus a Selective Serotonin Reuptake Inhibitor

In the previously noted chart-review study, the response rate to clomipramine augmentation of an SSRI or vice versa was 44.4% (n=4). This was higher than for the other augmentation strategies.[34] The effect size was small to medium, which was smaller than for the other augmentation strategies, although the power of the analysis was limited.

Antipsychotics

While antipsychotics alone do not appear effective for BDD (although data are limited to retrospective findings), antipsychotic augmentation of SRIs has considerable face validity, given that many patients have prominent delusions of reference and delusional conviction about the perceived appearance defect. In addition, this approach has been shown to be efficacious in OCD.[49] The only data on this strategy come from the aforementioned chart-review study, in which the response rate to antipsychotic augmentation was only 15.4% (n=2); however, the effect size for atypical antipsychotics was large.[34]

Other Agents

The previously noted chart-review study provides the only data on the use of other agents as SRI augmenters, in which the response rate to lithium augmentation of SRIs was 20% (n=1), with a large effect size, and the response rate to methylphenidate augmentation was 16.7% (n=1), also with a large effect size.[34] In addition to the notable improvement in BDD symptoms occasionally seen with these approaches, symptoms of depression or anergia may improve. This may in turn make BDD symptoms easier to tolerate. There are no published reports on the efficacy of bupropion or mirtazapine augmentation of SRIs, but in the author's experience they may sometimes be helpful for co-occurring depressive symptoms, but less effective for BDD symptoms. Venlafaxine augmentation of selective SRIs (SSRIs) also has some promise. These approaches warrant investigation.

A RECOMMENDED PHARMACOTHERAPEUTIC APPROACH TO THE PATIENT WITH BDD

The following recommendations are based on available data and are also informed by the author's clinical experience. Empirical evidence on effective pharmacotherapy for BDD, while dramatically increasing, is still limited. This is especially the case for augmentation strategies and treatment-resistant BDD. It should be kept in mind that the following recommendations are general suggestions that may require modification to appropriately treat an individual patient. Comorbidity, for example, may indicate the need for additional treatment, as in the case of type I bipolar disorder requiring a concomitant mood stabilizer. For certain patients with substance abuse or dependence, it may be unwise to use a benzodiazepine or a stimulant. A proposed algorithm for the pharmacotherapy of BDD, which is consistent with the following recommendations, has been published elsewhere.[50]

1) Recognize and diagnose BDD.

This is the first essential step to effective treatment. While this point may appear self-evident, studies indicate that although BDD is a relatively common disorder,[10,11] it is nearly always missed in clinical practice, in both inpatient and outpatient settings.[11,12] The diagnosis can be made using relatively straightforward questions which establish that the patient is preoccupied with nonexistent or minimal appearance flaws, which cause clinically significant distress or impairment in functioning.[2]

2) Provide psychoeducation about BDD.

Providing education about BDD is an important next step that often facilitates engagement of the patient in treatment. Web sites[51] and books[2] for the layperson may be helpful, especially because these patients may be reluctant to accept psychiatric care (because of their poor insight, desire for nonpsychiatric treatment such as surgery, or for other reasons). Other general aspects of treatment, such as the challenge of engaging delusional patients in treatment, involving family members in treatment, and collaborating with dermatologists or surgeons, are reviewed elsewhere.[52,55]

3) Use an SRI as a first-line approach, including for delusional patients.

The aforementioned data indicate that SRIs are effective for a majority of patients, including those who are delusional. Fluoxetine, clomipramine, fluvoxamine, and citalopram have received the most investigation, but sertraline and paroxetine appear effective. Although no controlled studies have directly compared one SRI with another, very preliminary data suggest that all SRIs have approximately equivalent efficacy.[34] Most clinicians would begin treatment with an SSRI rather than clomipramine, given the latter's greater propensity to cause side effects and toxicity in overdose.

4) Use the maximum SRI dose recommended or tolerated unless a lower dose is effective.

Although dose-finding studies have not been done, BDD appears to often require higher SRI doses than those typically used for depression. Doses reported in most published studies have been fairly high (eg, 77.7±8.0 mg/day in the fluoxetine study[39] and 238.3±85.8 mg/day in a fluvoxamine study[23]), but these studies used a forced-titration schedule with a relatively high target dose. Nonetheless, relatively high mean doses have also been used in the author's clinical practice, despite the fact that an attempt was often made to find the lowest effective dose: 66.7±23.5 mg/day for fluoxetine; 308.3±49.2 mg/day for fluvoxamine; 55.0±12.9 mg/day for paroxetine; 202.1±45.8 mg/day for sertraline; and 203.3±52.5 mg/day for clomipramine.[34]

Clinical experience indicates that some patients warrant and benefit from SSRI doses that exceed the maximum recommended dose—for example, 400 mg/day of fluvoxamine, 80–100 mg/day of citalopram, or 100 mg/day of paroxetine. These higher doses are best suited to patients with a partial response to the highest recommended dose who are tolerating the medication well, and patients who have failed many SSRIs. Clomipramine doses, however, should not exceed 250 mg/day because of seizure risk.

The rapidity of dose titration will depend on a number of factors, including illness severity (with quicker titration generally advisable for sicker patients, especially those who are suicidal), medication tolerability, and patient preference. Generally, however, it is advisable to reach the maximum recommended medication dose by weeks 5–9 of treatment, if tolerated. For example, in the fluoxetine study, patients received 20 mg/day for 2 weeks, with the dose raised by 20 mg/day every 10 days to a maximum dose of 80 mg/day, if tolerated (no patients dropped out of this study because of medication side effects).[39] In the citalopram study, 20 mg/day was initially prescribed, with the dose raised to 40 mg/day after 2 weeks and 60 mg/day after 4 weeks (KA Phillips, MD, and F Najjar, MD, unpublished data, 2001). This approach may result in treating with a higher SRI dose than is necessary, but it has the advantage of not missing a response because of undertreatment, and it also prevents an unnecessarily protracted-treatment trial that could result from slow titration.

5) Treat with an SRI for 12–16 weeks before making a final determination of efficacy.

Studies that have assessed time to SRI response have reported a mean time of 6–9 weeks and as long as 16 weeks.[23,33,35,39] The only exception is a recently completed study of citalopram that reported a mean time to response of only 4.6±2.6 weeks (KA Phillips, MD, and F Najjar, MD, unpublished data, 2001). In a fluvoxamine study, 6 (32%) of the 19 eventual responders had not responded by week 8, although most (94%) responded by 12 weeks.[23] Most studies used a fairly rapid titration schedule, so an even longer time to response might be expected with a slower dose increase. While it is possible that trials longer than 16 weeks would have an even higher success rate, longer durations have not been studied. In the author's clinical experience, however, onset of efficacy after 16 weeks appears unlikely. It is therefore recommended that the medication be changed at 12–16 weeks if an adequate dose has been reached and the response is inadequate at that time.

6) Continue an effective SRI for at least 1 year, if not longer.

No continuation, maintenance, or discontinuation studies have been done in BDD, so empirical data that might guide longer-term treatment are lacking. Nonetheless, in the author's clinical experience, relapse with continued treatment is rare, and many patients who respond by 12–16 weeks appear to experience further gradual improvement with continued pharmacotherapy. It is not clear whether further improvement is due to a direct effect of the medication, or to behavioral changes (eg, less social avoidance) made possible by medication response, which in turn facilitate further improvement. This phenomenon appears to be a continuation of an earlier response, rather than appearance of a new response.

The only data on relapse (from a chart-review study) indicate that relapse is likely with SRI discontinuation, occurring in 84% of patients.[34] It is unknown whether the relapse rate differs following different treatment durations. The recommendation to continue an effective SRI for at least 1 year is somewhat arbitrary, especially because the optimal treatment duration has not been systematically studied. It would seem wise to tailor the duration of treatment to the individual patient. For severely ill patients (eg, those with numerous, potentially lethal suicide attempts due to BDD), it is probably best to continue the medication for life. Patients who have had several relapses when discontinuing the medication may also need longer-term pharmacotherapy. In the author's experience, discontinued medication that was previously effective is usually effective with reinitiation, although occasional patients do not have as robust a response as with its initial use.

7) If an effective SRI is discontinued, discontinue it carefully.

Clinical experience suggests that if a decision is made to discontinue effective medication, it should be slowly tapered (eg, over months) rather than suddenly discontinued. Because the risk of relapse appears high, discontinuation should ideally be done at a time when the patient is not highly stressed and is able to tolerate a relapse if it occurs. Whether concomitant cognitive-behavior therapy reduces the risk of relapse with medication discontinuation is unknown and warrants investigation.

8) Do not simply treat depression.

A majority of patients with BDD have major depression, and many additional patients have depressive symptoms that do not qualify for a diagnosis of major depression.[14] A depressive disorder diagnosis and depressive symptoms often appear secondary to BDD (although this does not always seem to be the case). In the author's experience,

focusing treatment on depression but not BDD is a common clinical error. An effective regimen for depression will not necessarily effectively treat BDD; however, an effective regimen for BDD will usually effectively treat depression.[23,38,39]

As previously noted, although data are very limited, non-SRI antidepressants (with the possible exception of venlafaxine) appear ineffective as single agents for BDD. Non-SRI antidepressants also appear relatively ineffective for accompanying depressive symptoms, as indicated by a study by Hollander and colleagues[38] in which depressive symptoms were reduced more by clomipramine than by desipramine. This was also the case for subjects with a comorbid diagnosis of depression. This finding suggests that BDD is not simply a symptom of depression; if it were, desipramine should have been as effective as clomipramine. Another reason to not simply treat depression is that longer treatment trials and higher SRI doses than those usually used for depression are often needed to treat BDD symptoms. In addition, several[23,37] (although not all[39]), studies have found that relatively long trials may also be needed to treat depressive symptoms in BDD patients (7.0±4.6 weeks in one study[53] and more than 6 weeks in another.[37]

9) Try sequential SRIs if necessary.

Although all SRIs appear effective, one may be more effective than another for an individual patient. If one SRI fails, another should be tried, as some patients will respond. The author has treated a number of patients who responded to an SRI after failing all other SRIs, venlafaxine, and numerous augmentation strategies. In the only study to examine this question, of those subjects who failed an initial adequate SRI trial, 42.9% (n=6) responded to at least one subsequent adequate SRI trial, and 43.5% (n=10) of subsequent adequate SRI trials received by these subjects were effective.[34] Among responders to an initial SRI who were subsequently treated with a different SRI, 92.3% (n=12) of subsequent trials also led to improvement.[34]

10) Venlafaxine or an MAOI may be worth trying.

In the author's experience, venlafaxine may be effective for BDD. Although data on MAOIs are very limited, these agents appear less effective than SRIs but perhaps more effective than other antidepressants. Because of the risk of side effects and hypertensive crisis, it would seem best to restrict MAOI use to patients who have failed adequate trials of all of the SRIs and venlafaxine.

11) Avoid using antipsychotics as monotherapy, even for delusional patients.

As discussed in an earlier section, antipsychotics appear ineffective as single agents, even for delusional BDD patients. SRIs alone appear effective for these patients. This important issue, however, requires further investigation.

12) Consider buspirone, clomipramine, an antipsychotic, or other SRI-augmentation strategies.

Regarding the choice of an augmentation agent, no methodologically rigorous studies have compared one augmentation agent to another. Buspirone augmentation is appealing, however, because the medication is usually so well tolerated and relatively easy to prescribe. It may also improve concomitant anxiety and possibly depressive symptoms. Doses of 30–60 mg/day are recommended, and some patients benefit from an even higher dose (eg, 90 mg/day).[48]

As previously noted, clomipramine may also be effective and may be the preferred strategy for patients with severe depression comorbid with severe BDD. However, SSRI augmentation with clomipramine is riskier than with other augmentation approaches because SSRIs have the potential to unpredictably and sometimes dramatically increase blood levels of clomipramine, which has a low therapeutic index. Although this approach is generally well tolerated, patients should be followed closely for signs of toxicity. Clomipramine levels should be monitored (the author's practice is to check a clomipramine level at a dose of 25 mg/day or 50 mg/day after adding it to an SSRI). Clomipramine and an SSRI generally should not be combined without first attempting to maximize a trial with one of them.

Antipsychotic augmentation of an SRI appears less often effective than buspirone or clomipramine augmentation, but the evidence is too limited at this time to draw any firm conclusions about the comparative efficacy of these approaches. This approach would seem reasonable for delusional patients who fail an SRI or for severely ill delusional patients as initial treatment in combination with an SRI. It is unknown whether atypical antipsychotics are more effective than typical antipsychotics, including pimozide, but they are likely to be better tolerated. It is possible that neuroleptic augmentation is more effective for patients who perform tic-like behaviors, such as skin-picking or hair-plucking, though this question has not been investigated.

Adding lithium or a stimulant appears more effective for depressive than BDD symptoms, but diminishing depressive symptoms is clearly beneficial and may also help patients better tolerate BDD symptoms. Although it is theoretically possible that skin-picking, a tic-like behavior, might worsen with stimulant treatment, the author has not seen this occur.

What constitutes an adequate augmentation trial is unclear, but a duration of 6–8 weeks is probably adequate to determine whether the approach will be effective. It is probably best to use a 12-week trial for clomipramine augmentation.

13) Is it better to augment an SRI or switch to another SRI?

The answer to this question is unclear. The only study to date that sheds any light on this issue found that in patients who had failed an adequate SRI trial, 43.5% (n=10) of subsequent adequate SRI trials were effective versus 33.3% (n=8) of various SRI-augmentation strategies.[34] However, 40.5% (n=15) of augmentation trials were successful in partial SRI responders.[34] The relatively small number of trials and the study's methodological limitations preclude drawing a firm conclusion about which approach is more effective. From a clinical perspective, if a patient has failed three SRI

trials without any attempt at augmentation, it would seem that augmentation should be tried. Conversely, if a patient has failed several augmentation strategies with one SRI, a switch to another SRI should be considered. Numerous factors need to be considered, however. For example, the better the SRI response, the less appealing it would be to discontinue it and try another SRI. Augmentation may also be more appealing if there is a high risk of serious consequences due to relapse, which could occur when switching from a partially effective SRI.

14) Consider benzodiazepine use for agitated or anxious patients.

Because patients with BDD can be extremely distressed, anxious, and agitated, adjunctive benzodiazepine use should be considered. This approach may be used for a short duration (eg, until an SRI begins to work) or for the longer term if clinically indicated. Benzodiazepines may enable treatment with an SRI if an SRI causes agitation. A benzodiazepine, by alleviating anxiety and insomnia, can make BDD symptoms more tolerable. It is also possible that benzodiazepines may have a more direct effect on BDD symptoms, although in the author's experience, this effect, if it occurs at all, tends to be minimal. Clonazepam, which may have serotonergic properties[54] and possibly be effective for OCD,[1] may be preferable to other benzodiazepines, although this question has not been studied. The potential for substance abuse or dependence must be considered, although in the author's clinical experience, relatively few patients abuse these medications.

15) Consider cognitive-behavior therapy.

Although the efficacy of cognitive-behavior therapy is beyond the scope of this review, it is worth noting that this treatment approach should also be considered.[55] There are no data available to address the question of whether pharmacotherapy or cognitive-behavior therapy are more effective, or whether combining these treatments is more effective than using either one alone. In the author's experience, these approaches are complementary. For example, partial response to an SRI can make it possible for a severely depressed, delusional, or suicidal patient to engage in and tolerate cognitive-behavior therapy. In the author's opinion, medication is always indicated for severely ill, severely depressed, or highly suicidal patients.

FUTURE PHARMACOTHERAPY RESEARCH NEEDS

Virtually all aspects of pharmacotherapy for BDD need to be studied, as research in this area is still in its early stages. One of the most pressing needs is for additional placebo-controlled SRI trials, including trials that compare SRIs to other medication classes, such as non-SRI antidepressants, to determine whether SRIs are truly preferentially efficacious for BDD. Because patients typically experience a partial response, rather than remission, with SRIs, it is also critically important to evaluate pharmacologic augmentation strategies in a methodologically rigorous way, so that treatment response can be optimized. Equally compelling is the need to evaluate cognitive-behavior therapy as an SRI "augmentation" strategy. Another important avenue of research is to compare the efficacy of cognitive-behavior therapy versus SRIs versus their combination to determine which treatments are most effective for which patients.

The longest systematic pharmacotherapy study to date was only 16 weeks in duration, making continuation and maintenance studies necessary to confirm clinical impressions that SRI response is generally maintained, and may even further improve, with longer-term treatment. Because BDD can be so severely distressing and impairing, the likelihood of relapse with medication discontinuation is a particularly important question; the only published data on this issue come from a single chart-review study, underscoring the need for rigorous placebo-controlled, relapse-prevention studies. Once studies such as the above more firmly establish which pharmacotherapeutic approaches are efficacious for BDD, effectiveness studies are needed that evaluate the usefulness of medications under "real world" conditions (eg, for patients in community settings who are not excluded because of comorbid conditions, such as substance abuse). Finally, elucidation of BDD's underlying neurobiology, which to date has received virtually no investigation, may provide fruitful leads for new pharmacologic approaches to the treatment of this disorder.

CONCLUSION

As recently as a decade ago, virtually nothing was known about effective pharmacotherapy for BDD. Pharmacologic approaches for BDD have received far less investigation than for many other common and severe mental disorders, and much remains to be learned. At the same time, our knowledge of effective pharmacologic treatment for BDD has dramatically increased to the point where a majority of patients with this relatively common disorder may obtain relief from their distressing and often disabling illness. CNS

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