A Randomized Placebo-Controlled Trial of Fluoxetine in Body Dysmorphic Disorder

Katharine A. Phillips, MD; Ralph S. Albertini, MD; Steven A. Rasmussen, MD

Background: Research on the pharmacotherapy of body dysmorphic disorder (BDD), a common and often disabling disorder, is limited. Available data suggest that this disorder may respond to serotonin reuptake inhibitors. However, no placebo-controlled treatment studies of BDD have been published.

Methods: Seventy-four patients with DSM-IV BDD or its delusional variant were enrolled and 67 were randomized into a placebo-controlled parallel-group study to evaluate the efficacy and safety of fluoxetine hydrochloride. After 1 week of single-blind placebo treatment, patients were randomized to receive 12 weeks of double-blind treatment with fluoxetine or placebo. Outcome measures included the Yale-Brown Obsessive Compulsive Scale Modified for Body Dysmorphic Disorder (BDD-YBOCS) (the primary outcome measure), the Clinical Global Impressions Scale, the Brown Assessment of Beliefs Scale, and other measures.

Results: Results of the BDD-YBOCS indicated that fluoxetine was significantly more effective than placebo for BDD beginning at week 8 and continuing at weeks 10 and 12 ($F_{1,64}=16.5; P<.001$). The response rate was 18 (53%) of 34 to fluoxetine and 6 (18%) of 33 to the placebo ($\chi^2=8.8; P=.003$). The BDD symptoms of delusional patients were as likely as those of nondelusional patients to respond to fluoxetine, and no delusional patients responded to the placebo. In the sample as a whole, treatment response was independent of the duration and severity of BDD and the presence of major depression, obsessive-compulsive disorder, or a personality disorder. Fluoxetine was generally well tolerated.

Conclusion: Fluoxetine is safe and more effective than placebo in delusional and nondelusional patients with BDD.

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Body dysmorphic disorder (BDD), also known as dysmorphophobia, consists of a distressing or impairing preoccupation with an imagined or slight defect in appearance. Although BDD was first described more than a century ago, research on its pharmacologic treatment remains limited and no placebo-controlled pharmacotherapy studies have been done to our knowledge. Such research is needed since BDD causes severe distress and marked impairment in functioning. A high percentage of patients require hospitalization, become housebound, and attempt suicide. Committed suicide has been reported in both psychiatric and dermatologic settings, and quality of life is notably poor.

Body dysmorphic disorder seems to be relatively common in community, psychiatric, cosmetic surgery, and dermatologic settings. As many as 50% of patients with BDD receive surgery or dermatologic treatment, often with poor outcomes. In all of these settings, BDD has been reported to be extremely difficult to treat.

Early case reports noted mixed but largely negative outcomes with a variety of psychotropic agents and electroconvulsive therapy. However, subsequent data from case series and 2 open-label fluvoxamine maleate trials suggest that BDD may respond to serotonin reuptake inhibitors (SRIs). The only published controlled pharmacotherapy trial on BDD to our knowledge was a double-blind crossover study, which found that the SRI clomipramine hydrochloride was more effective than the non-SRI antidepressant desipramine hydrochloride, supporting earlier retrospective findings that SRIs may be selectively effective for BDD and that the treatment response of BDD differs from that of depression.

Most patients with BDD have poor insight or are delusional regarding their appearance flaws, which has the potential to complicate treatment. Available data suggest that patients with delusional BDD respond to SRIs as well or even better than
PATIENTS AND METHODS

PATIENTS

The study was done in outpatients at a single academic site. Patients were entered into the study from August 1995 through February 2000. All patients met DSM-IV criteria for BDD: (1) preoccupation with an imagined defect in appearance; if a slight physical anomaly is present, the person's concern is markedly excessive; (2) the preoccupation causes clinically significant distress or impairment in social, occupational, or other important areas of functioning; and (3) the preoccupation is not better accounted for by another mental disorder (eg, dissatisfaction with body shape and size in anorexia nervosa). Because the Structured Clinical Interview for DSM-III-R (SCID-P)31,32 did not include BDD, BDD was diagnosed with the Body Dysmorphic Disorder Diagnostic Module, a reliable semistructured SCID-like diagnostic instrument based on DSM-IV criteria.33 Patients with delusional beliefs about their appearance (delusional disorder, somatic type) were included because the delusional and nondelusional forms of BDD seem to constitute the same disorder,7 and patients with delusional BDD may be diagnosed with both BDD and delusional disorder according to the DSM-IV33 (patients with other types of somatic delusions but no appearance-related delusions were excluded). Body dysmorphic disorder was diagnosed by the consensus of the first 2 authors. A family member or other informant was interviewed (for the 36 patients willing and able to do this); in all cases, the BDD diagnosis was confirmed. Comorbid disorders were diagnosed by the first author with the SCID-P and the Structured Clinical Interview for DSM-III-R Personality Disorders.37 Data on the clinical characteristics of BDD were obtained with a semistructured instrument (K.A.P., unpublished data, 1992).

Inclusion criteria were (1) presence of DSM-IV BDD or its delusional variant currently and for at least 6 months; (2) age 18 to 65 years; (3) score of 24 or higher on the Yale-Brown Obsessive Compulsive Scale Modified for Body Dysmorphic Disorder (BDD-YBOCS);38 (4) score of at least moderate on the Clinical Global Impression Scale for BDD (BDD-CGI);39 (5) ability to communicate and give written informed consent.

Exclusion criteria were (1) schizophrenia, schizoaffective disorder, or another current or lifetime psychotic disorder not attributable to delusional BDD; (2) current or lifetime bipolar disorder; (3) alcohol or substance dependence or abuse in the past 6 months; (4) body image concerns better accounted for by an eating disorder, including eating disorder not otherwise specified; (5) primary body image concern with weight and BDD criteria not met if weight concerns

nondelusional patients, although most studies did not assess delusionality (insight) with a reliable and valid scale. In addition, several studies found that delusionality improves with SRI treatment.31,32 Although data are very limited, antipsychotics alone seem ineffective for delusional BDD.3,7

We report the first placebo-controlled treatment study of BDD and its delusional variant. We hypothesized that (1) fluoxetine hydrochloride would be more effective than placebo (the primary hypothesis); (2) delusional BDD would respond as well as nondelusional BDD to fluoxetine; and (3) illness severity and the presence of major depression, obsessive-compulsive disorder (OCD), or a personality disorder would not predict outcome.

RESULTS

PATIENT SAMPLE DESCRIPTION

Of the 74 enrolled patients, 6 were discontinued from the study during the screening period and 1 was discon-
tinued after the single-blind placebo lead-in week because her BDD-YBOCS score decreased to less than 24 (Figure 1). No patients responded to the single-blind placebo. Sixty-seven patients were randomized to receive double-blind treatment with fluoxetine (n = 34) or placebo (n = 33). Three patients (9%) randomized to receive fluoxetine and 5 (15%) randomized to receive placebo discontinued study participation ($\chi^2 = 0.64, P = .42$).

There were no significant differences between the fluoxetine (n = 34) and placebo (n = 33) groups on base-line demographic and clinical characteristics (Table 1). For example, skin (eg, acne) and hair (eg, hair loss) were the most common appearance concerns (skin: 25 [74%] in the fluoxetine group and 26 [79%] in the placebo group; hair: 14 [41%] in the fluoxetine group and 19 [58%] in the placebo group). Twelve patients (37.5%) in the fluoxetine group and 15 patients (46.9%) in the placebo group were delusional at baseline. Ongoing psychotherapy (begin before study entry) was received during the study by 3 patients in the fluoxetine group and 3 patients in

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TREATMENT OUTCOME OF BDD

Fluoxetine was superior to placebo for BDD symptoms as measured by the primary and secondary BDD outcome measures and both clinician and patient ratings (Table 2). Controlling for baseline group differences in BDD severity, on the BDD-YBOCS (the primary outcome measure), fluoxetine was more effective than placebo \(F_{1,56} = 16.5; P < .001\) beginning at week 8 \(F_{2,56} = 4.63; P = .04\) and continuing at weeks 10 and 12. The mean change from baseline in the BDD-YBOCS total score was more than twice as large with fluoxetine as with placebo treatment (35% vs 14% decrease; \(t_{35} = 3.54; P = .003\)), with a similar decrease for BDD preoccupations and repetitive behaviors. The response rate on the BDD-YBOCS to fluoxetine was 53% (18/34) vs 18% (6/33) to placebo \(\chi^2 = 8.8; P = .003\). The treatment effect size was medium to large \((f = 0.35; 95\% \text{ confidence interval, 0.22-0.48; } d \text{ equivalent = 0.70} )\).

On the clinician-rated BDD-CGI, 14 patients (41%) treated with fluoxetine were much improved and 5 (15%) were very much improved. Functional impairment as assessed by the GAF and SOFAS improved more with fluoxetine than placebo (Table 2).

The mean ± SD time to fluoxetine response (as assessed by a 30% decrease in BDD-YBOCS score) was 7.7 ± 3.5 (range, 2-12) weeks and to placebo was 5.3 ± 3.2 (range, 1-8) weeks \((t_{30} = 1.97; P = .04)\). The mean ± SD fluoxetine dose at end point was 77.7 ± 8.0 (range, 40-80) mg/d; the fluoxetine equivalent in the placebo group was 76.0 ± 13.1 (range, 20-80) mg/d.

Of the 21 patients treated with open-label fluoxetine after placebo treatment during the double-blind phase (mean ± SD fluoxetine dose at end point, 61.1 ± 21.4 mg/d), 5 (24%) responded to the BDD-YBOCS. Scores decreased from a mean ± SD score of 29.3 ± 7.4 to 22.3 ± 7.2 \((t_{20} = 5.14; P < .001)\). On the clinician-rated BDD-CGI, 9 (43%) responded, with 7 (33%) much improved and 2 (10%) very much improved.

In 34 cases (69%), the clinician correctly judged whether the patient had received fluoxetine or placebo; this was the case for 25 (63%) patients. The clinician’s judgment was incorrect in 6 (12%) cases and the patient’s in 10 (23%). The clinician was unsure of group assignment in 9 (18%) of cases and the patient in 5 (13%).

OUTCOME IN DELUSIONAL AND NONDELUSIONAL PATIENTS

We tested for a difference in the amount of improvement in BDD symptoms from baseline to end point for delusional \((n = 27)\) vs nondelusional \((n = 37)\) patients, covary-
End Point

were nondelusional at baseline to respond to fluoxetine were as likely as those of patients who had severe BDD symptoms at baseline (delusional patients’ mean ± SD BDD-YBOCS scores, 33.0 ± 5.1; nondelusional patients, 29.4 ± 5.6; t120 = 2.65; P = .01), an ANCOVA that controlled for BDD severity at baseline indicated that this did not account for their lower placebo response rates (Table 2). However, BDD symptoms of delusional patients were significantly less likely than those of nondelusional patients to respond to placebo (0% [0/15] vs 35% [6/17]; χ² = 6.51; P = .01). Although delusional patients had more severe BDD symptoms at baseline (delusional patients’ mean ± SD BDD-YBOCS scores, 33.0 ± 5.1; nondelusional patients, 29.4 ± 5.6; t120 = 2.65; P = .01), an ANCOVA that controlled for BDD severity at baseline indicated that this did not account for their lower placebo response rates (F1,61 = 1.91; P = .17). In delusional patients, the response rate of BDD symptoms to fluoxetine was significantly higher than to placebo (50% vs 0%; χ² = 9.6; P = .002). This was not the case for nondelusional patients (55% vs 35%; χ² = 1.44; P = .23), although power was limited (1−β = .27).

We also examined a second question: with treatment, did patients’ conviction that their appearance was abnormal (delusional) change with fluoxetine compared with placebo treatment? While Brown Assessment of Beliefs Scale scores decreased between baseline and end point for both the fluoxetine and placebo groups, the difference between them was not significant (Table 2). However, scores decreased significantly more in treatment responders than in treatment nonresponders (for both treatment groups combined (F3,8,233,6 = 9.5; P < .001).

Table 2. Baseline and End Point Efficacy Measures by Treatment Group *

<table>
<thead>
<tr>
<th>Measure</th>
<th>Baseline (n = 33)</th>
<th>Placebo (n = 33)</th>
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*Data are given as mean ± SD unless otherwise indicated. BDD-YBOCS indicates Yale-Brown Obsessive Compulsive Scale Modified for Body Dysmorphic Disorder; CGI, Clinical Global Impressions Scale; BDD-NIMH, National Institute of Mental Health Global Obsessive Compulsive Scale modified for BDD; HAM-D, Hamilton Rating Scale for Depression (17-item); BPRS, Brief Psychiatric Rating Scale; GAF, Global Assessment of Functioning Scale; SOFAS, Social and Occupational Functioning Scale; and ellipses, not applicable.

OUTCOME OF DEPRESSION

Hamilton Rating Scale for Depression scores improved significantly more with fluoxetine than with placebo (Table 2). Change in BDD-YBOCS and HAM-D scores was correlated r = 0.65 (P < .001) for the fluoxetine group and r = 0.58 (P < .001) for the placebo group. Two patients (6%) treated with fluoxetine and 10 (30%) treated with placebo had an increase (ie, worsening) on the HAM-D suicidal ideation item between baseline and end point (P = .001).

PREDICTORS OF TREATMENT OUTCOME

In the entire sample, BDD duration, BDD severity, and the presence of a personality disorder, current OCD, or current major depression did not predict response of BDD in a stepwise regression analysis. Furthermore, with regard to depression, there was no main effect of the diagnosis of major depression at baseline on BDD outcome (F1,65 = 1.0; P = .32) and no interaction between major

Figure 2. Scores over time on the Yale-Brown Obsessive Compulsive Scale Modified for Body Dysmorphic Disorder (BDD-YBOCS) by treatment group for the intent-to-treat sample (n = 67). Last observation carried forward ANCOVA (controlling for baseline BDD-YBOCS): F1,65 = 16.5, P < .001. Response to placebo = 6/33 (18.2%) vs fluoxetine = 18/34 (52.9%) χ² = 8.8, P = .003. The asterisk indicates the 2 groups significantly differed beginning at this time point (P = .04). Bars represent 1 SE.

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SAFETY AND TOLERABILITY

Treatment-emergent adverse events (irrespective of relationship to study drug) were reported by 82% of patients (n=28) treated with fluoxetine and 64% (n=21) treated with placebo (χ² = 3.0; P = .08). The only adverse events that were significantly more frequent with fluoxetine treatment were drowsiness and stomach/abdominal discomfort (Table 3). Five patients (7%) took chloral hydrate for insomnia. Adverse events were often transient, and nearly all were of mild to moderate severity and well tolerated. No patients discontinued the study because of adverse events. No serious adverse events (eg, suicide attempts or hospitalizations) occurred.

COMMENT

This study, the first placebo-controlled trial on BDD, indicates that fluoxetine is safe and more effective than placebo for BDD, including delusional patients. Fluoxetine was more effective for BDD on the primary and secondary BDD outcome measures and as assessed by both clinician and patient ratings, with a medium to large effect size. Depressive symptoms, global symptomatology, and functioning also improved significantly more with fluoxetine than with placebo.

Consistent with previous studies, fluoxetine was as effective for BDD symptoms in delusional as in nonde-
response rate to subsequent open-label fluoxetine (compared with double-blind fluoxetine) might be expected.

This study has several limitations characteristic of efficacy trials. It was conducted in a university-affiliated private psychiatric hospital, and the sample was selected to meet strict inclusion and exclusion criteria. Patients with milder BDD symptoms were excluded as were patients who were highly suicidal or who needed inpatient treatment. Future studies are required to determine how generalizable the results are to other populations of patients with BDD. Another limitation is that a longer treatment trial might have yielded a slightly higher fluoxetine response rate since an open-label fluvoxamine trial found that 5.3% of respondents required more than 12 weeks to respond.29

These results, while promising, require replication. Placebo-controlled studies of other SRIs and parallel-group studies comparing SRIs with other medications (eg, antipsychotics) are needed, as are longer-term treatment studies (eg, continuation and maintenance studies), especially because BDD seems to be a chronic illness.7 While it is our clinical impression that the response of BDD to SRIs is usually maintained or further increases over time with continued treatment, this impression requires empirical validation. It is worth underscoring that only slightly more than half of patients responded to fluoxetine, and even though their response was clinically significant, it was usually partial. It is therefore critically important to determine whether adding other pharmacologic agents or psychotherapy (eg, cognitive-behavioral therapy) to fluoxetine or other SRIs might enhance treatment outcome. In the meantime, this study suggests that fluoxetine is a safe and effective treatment for BDD—a distressing, relatively common, and severe mental disorder.

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