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Suicidality in a Placebo-Controlled Fluoxetine Study of Body Dysmorphic Disorder

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Abstract

Objectives—SRIs are considered the first-line medication for body dysmorphic disorder (BDD). The relationship between SRI treatment and suicidality in BDD has been only minimally studied, despite high suicidality rates in BDD.

Methods—Sixty-seven adults with DSM-IV BDD participated in a 12-week randomized double-blind placebo-controlled study of fluoxetine. Suicidality was assessed with the HAM-D suicidal ideation item. Analyses examined group differences in worsening and emergence of suicidality, using standard definitions.

Results—Among the entire sample, when comparing study baseline to end of week 2 and study endpoint, no subject on fluoxetine had suicidality worsening; a higher proportion of placebo-treated subjects had suicidality worsening after two weeks of treatment (p = .014) and at study endpoint (p = .010). Among subjects age 18–24, one subject on placebo had suicidality worsening at the end of week 2, and none in either treatment group had suicidality worsening at study endpoint. Regarding emergence of suicidality at any point during the study, the treatment groups did not significantly differ. No suicide attempts or completed suicides occurred.

Conclusions—Fluoxetine and placebo did not significantly differ with regard to emergence of suicidality. Among the entire sample, fluoxetine appeared to exert a protective effect against suicidality worsening.

Keywords

body dysmorphic disorder; dysmorphophobia; suicidality; suicide; fluoxetine; treatment; clinical trial

Introduction

Individuals with body dysmorphic disorder (BDD), a distressing or impairing preoccupation with an imagined or slight defect in appearance, appear to have markedly elevated suicidality rates. Approximately 80% report a history of suicidal ideation, and 24%–28% have attempted suicide. The annual rate of completed suicide (0.3%), while very preliminary, appears higher than for nearly all other mental disorders (Phillips, 2007).

It is important to investigate change in suicidality with SRI treatment, as SRIs are considered the first-line medication for BDD (National Collaborating Centre for Mental Health, 2006; Phillips and Hollander, 2008). Our clinical experience suggests that suicidality in BDD often

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decreases with SRIs. Some short-term studies of other disorders, however, suggest that SRIs may be associated with increased suicidality in children (FDA, 2007; NHS, 2008) and young adults up to age 24 (FDA, 2007).

Suicidality with SRI treatment in BDD has been only minimally studied. Reports are limited to a small open-label escitalopram study in BDD (n=15), in which mean scores on the Hamilton Depression Rating Scale suicidality item significantly decreased (p = .001) (Phillips, 2006). In the only placebo-controlled SRI study in BDD, suicidality among the entire sample was noted to be worse at study endpoint in the placebo than the fluoxetine group (Phillips et al., 2002). However, that study did not further examine change in suicidality. This report presents additional secondary analyses from the placebo-controlled fluoxetine study which examine suicidality worsening, suicidality emergence, and symptoms that might be precursors to suicidality worsening or emergence (FDA, 2007).

Methods

Sixty-seven outpatients age 18 and older (mean age=32.1±10.5 years; 68.7% women) with DSM-IV BDD participated in a 12-week randomized placebo-controlled parallel-group study of fluoxetine's efficacy for BDD. (The study's methods and primary results were reported in Phillips et al., 2002). Inclusion/exclusion criteria were standard for efficacy trials. Individuals were excluded if they had a recent suicide attempt or clinically significant suicidal ideation. Subjects were assessed weekly for the first four weeks of the study and then every other week. The hospital Institutional Review Board approved the study, and subjects provided written informed consent.

Suicidality during the past week was assessed with the suicidal ideation item from the 17-item Hamilton Rating Scale for Depression (HAM-D) (Miller et al., 1985). Standard definitions were used for worsening and emergence of suicidality (Hammad et al., 2006). *Suicidality worsening* was defined as an increase of 1 or more points on the HAM-D suicide item between baseline and study endpoint. Worsening was also examined between baseline and the end of two weeks of treatment because increased risk of suicidality appears greatest during this time period (Jick et al., 2004). *Emergence of suicidality* was defined as an increase from a score of 0 or 1 at baseline to a 2 or higher on this item at any point during the study. HAM-D items assessing depressive symptoms, insomnia, agitation, and anxiety were examined, because these symptoms (among others) might be precursors to suicidality worsening or emergence (FDA, 2007). Hopelessness was also examined, as it has also been strongly associated with suicidality (Glanz et al., 1995). The Yale-Brown Obsessive-Compulsive Scale Modified for BDD assessed current BDD severity (Phillips et al., 1997).

Chi square analyses examined group differences in suicidality worsening and emergence. Repeated measures analysis of variance examined between-group differences in change in possible suicidality precursors. Analyses were intention-to-treat with last observation carried forward, except for analyses of suicidality worsening after two weeks, which include only subjects who completed two weeks of treatment.

Results

At baseline, subjects in the fluoxetine and placebo groups did not significantly differ with regard to BDD severity [$t(66) = -0.52$, p = .606], HAM-D total score [$t(66) = -0.89$, p = .377], or HAM-D suicide item score [$t(64) = 1.27$, p = .209]. Among the entire sample, compared to baseline no subject on fluoxetine had suicidality worsening at end of week 2 or at study endpoint; a significantly higher proportion of subjects taking placebo had suicidality worsening at both time points (p = .014 after two weeks and p = .010 at study endpoint) (Table 1).

Among subjects age 18–24, no one taking fluoxetine and only one taking placebo had suicidality worsening after two weeks of treatment; at endpoint no subject in either treatment group had greater suicidality than at baseline.

Regarding emergence of suicidality at any point during the study, the treatment groups did not significantly differ, either among the entire sample or among subjects age 18–24 (Table 1). One subject on placebo was removed early from the study because of emergence of substantial suicidality. No subjects attempted or completed suicide during the study.

Compared to the placebo group, the fluoxetine group had a significantly greater decrease in depressive symptoms and improvement in hopelessness between baseline and endpoint [$F(1, 65) = 6.10$, $p = .016$, and $F(1, 64) = 5.16$, $p = .026$, respectively]. The treatment groups did not significantly differ with regard to change in other possible suicidality precursors (insomnia, agitation, anxiety).

Discussion

Fluoxetine was not associated with worsening or emergence of suicidality in BDD, a disorder with a high risk of suicidality. In fact, among the entire sample, fluoxetine appeared to exert a protective effect against suicidality worsening. This result is consistent with recent studies in other disorders suggesting that antidepressants are associated with a decrease, rather than an increase, in suicidality (e.g., Gibbons et al., 2007; Simon and Savarino, 2007). Nor was fluoxetine associated with worsening or emergence of suicidality among young adults.

A high proportion of subjects, especially young adults on placebo (29%), experienced emergence of suicidality, despite the study's brief duration. This underscores the importance of carefully monitoring BDD patients for suicidality.

Study results may not apply to children under 18, who were not eligible for study participation. More highly suicidal individuals were also excluded, because placebo was used. Because patients with BDD appear at high risk of suicide, research is needed in larger samples using standardized suicidality measures.

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Table 1

Worsening and Emergence of Suicidality in Patients Treated with Fluoxetine Versus Placebo

Variable	Fluoxetine (n=34)	Placebo (n=33)	Statistic	*p*
Worsening of Suicidality				
End of second week of treatment				
All subjects (% within group)	0 (0)	5 (17)	$X2 = 6.01$	.014
Ages 18–24† (% within group)	0 (0)	1 (14)	$X^2 = 1.52$	.218
Study endpoint				
All subjects (% within group)	0 (0)	6 (19)	$X^2 = 7.01$	.010
Ages 18–24† (% within group)	0 (0)	0 (0)	--	--
Emergence of Suicidality				
All subjects (% within group)	4 (12)	6 (19)	$X^2 = 0.63$	.429
Ages 18–24† (% within group)	2 (17)	2 (29)	$X^2 = 0.38$	.539

† *Note*. n = 17 at end week 2 (fluoxetine, n= 10; placebo, n = 7) and n = 19 for the end week 12 (study endpoint) intent-to-treat sample (fluoxetine, n= 12; placebo, n = 7).