Citalopram in the Treatment of Binge-Eating Disorder: A Placebo-Controlled Trial

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Background: Binge-eating disorder is a newly recognized eating disorder characterized by recurrent episodes of binge eating without compensatory weight loss behaviors. It commonly co-occurs with depressive disorders and obesity. Citalopram is a highly selective serotonin reuptake inhibitor antidepressant. The purpose of this study was to assess the efficacy and safety of citalopram in the treatment of binge-eating disorder.

Method: Thirty-eight outpatients with a DSM-IV diagnosis of binge-eating disorder were enrolled in the study between August 2000 and July 2001 and were randomly assigned to receive either citalopram (N = 19) or placebo (N = 19) in a 6-week, double-blind, flexible-dose (20–60 mg/day) study. The primary measure of efficacy was frequency of binge-eating episodes. Secondary measures included frequency of binge days, body mass index (BMI), weight, Clinical Global Impressions-Severity of Illness scale scores, Yale-Brown Obsessive Compulsive Scale Modified for Binge Eating (YBOCS-BE) scores, Hamilton Rating Scale for Depression (HAM-D) scores, and response categories. The outcome measures were analyzed using 2 random regression methods, with a time trend analysis (primary analysis) and an endpoint analysis. In addition, response categories were analyzed using an exact trend test.

Results: Compared with placebo-treated subjects, subjects receiving citalopram (mean dose of 57.9 mg/day) had a significantly greater rate of reduction in frequency of binge eating ($p = .003$), frequency of binge days ($p < .001$), BMI ($p < .001$), weight ($p < .001$), severity of illness ($p = .028$), and YBOCS-BE score ($p = .007$) and a marginally significant rate of reduction in HAM-D score ($p = .053$). Differences between groups in response categories were marginally significant ($p = .068$ for intent-to-treat analysis).

Conclusion: In a 6-week, placebo-controlled, flexible-dose trial, citalopram was efficacious in reducing binge-eating frequency, weight, and severity of illness and was generally well tolerated in subjects with binge-eating disorder.

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Binge-eating disorder is characterized by recurrent, distressing, and uncontrollable episodes of excessive food consumption without compensatory weight loss behaviors.[1,2] Its prevalence in the general population of the United States is estimated to be 1.5% to 2%.[2–5] Binge-eating disorder is frequently associated with psychiatric comorbidity, most commonly depressive disorders,[5–7] and obesity.[2–5,8] Indeed, a substantial proportion of individuals presenting for weight management have binge-eating disorder, including approximately 8% to 30% of those seeking standard weight loss treatments,[2–4] up to 50% of those seeking bariatric surgery,[9,10] and 70% of those participating in Overeaters Anonymous.[3]

Although binge-eating disorder has no established psychopharmacologic treatment,[11,12] serotonin selective reuptake inhibitors (SSRIs) hold promise because the SSRI fluoxetine has been proved superior to placebo in reducing binge-purge episodes in the related condition bulimia nervosa in two 8-week double-blind trials,[13,14] one 16-week double-blind trial,[15] and one 52-week double-blind continuation trial.[16] Additionally, the SSRIs fluvoxamine,[17] sertraline,[18] and fluoxetine[19] have each been found superior to placebo in reducing binge-eating episodes and overweight in outpatients with binge-eating disorder in trials ranging from 6 to 9 weeks. Because of these observations, we conducted a placebo-controlled, randomized trial to assess the safety and efficacy of citalopram, the most selective SSRI presently available,[20,21] in binge-eating disorder.

METHOD

Study Design

The study was a single-center, parallel-group, randomized, placebo-controlled, double-blind, forced titration, flexible-dose study. After a week of single-blind placebo administration, subjects were randomly assigned to therapy with citalopram or placebo for a 6-week treatment period. All medications were dispensed in identical capsules (20 mg of citalopram or placebo). Subjects began randomized treatment with 20 mg/day for the first 7 days. The dosage was then increased, as tolerated, to 40 mg/day for 7 days, and then 60 mg/day for the remainder of the study. Study medication could be reduced to a minimum of 1 capsule (20 mg) daily because of intolerable side effects at any time during the 6-week treatment period.

Subject Selection Criteria

Subjects were outpatients who were recruited from advertisements for a binge-eating medication trial. Subjects were eligible for the study if they met DSM-IV criteria for binge-eating disorder[1] and had also experienced ≥ 3 binge-eating episodes weekly for at least the prior 6 months. Subjects were between 18 and 60 years of age and weighed more than 85% of their ideal body weight.[22] Subjects were excluded if they were pregnant or lactating; had concurrent anorexia nervosa or bulimia nervosa; had concurrent or recent (within 1 year of study entry) substance abuse or dependence; had a lifetime history of psychosis, mania or hypomania, or dementia; had a history of any psychiatric disorder that could interfere with diagnostic assessment, treatment, or compliance; posed a significant suicide risk; had received psychotherapy or behavioral therapy within 3 months of entry into the study; had clinically unstable medical illness; had a history of seizures; had clinically significant laboratory abnormalities; had received monoamine oxidase inhibitors within 4 weeks of randomization; had received other psychotropic medication within 2 weeks of randomization; had received investigational medications or depot neuroleptics within 3 months of randomization; had previously been treated with citalopram; or had experienced < 3 binges in the week before randomization (i.e., were considered placebo responders).

Subject Evaluation

The Institutional Review Board at the University of Cincinnati College of Medicine (Cincinnati, Ohio) approved the protocol, and all subjects provided written informed consent before administration of any study procedures. All subjects underwent a screening evaluation that included an interview for demographic information and medical, psychiatric, and family histories; the Structured Clinical Interview for DSM-IV[23] (to establish the diagnosis of binge-eating disorder and determine comorbid Axis I diagnoses); a physical examination; vital signs; height and weight; and routine blood chemical and hematologic tests. At this evaluation and each of the following visits, subjects were given take-home diaries in which to record any binges and, once medication was initiated, the number of capsules taken. Subjects were seen weekly during the study.

At each visit following the screen visit, subjects were assessed for number of binges experienced since the last visit, other outcome measures (except for the 17-item Hamilton Rating Scale for Depression [HAM-D],[24] which was administered at baseline and weeks 2, 4, and 6; see below), medication dose, medication compliance ascertained by capsule count, adverse events, use of nonstudy medications, vital signs, and weight.

Outcome Measures

The primary outcome measure was the weekly frequency of binge-eating episodes (binge frequency). A binge was defined using DSM-IV criteria.[1] Binges were assessed via clinical interview and review of subject take-home diaries, in which subjects recorded binges, duration of binges, and food consumed during binges (so that binges could be confirmed by the investigator). (Of note, the interviews and diary reviews were performed by the physician investigator [S.L.M., S.M., E.N., or P.E.K.] working with that particular subject.) Secondary outcome measures were weekly frequency of binge days (days during which there were 1 or more binges), body mass index (BMI; body weight in kilograms divided by height in meters squared), weight, Clinical Global Impressions-Severity of Illness scale (CGI-S) scores,[25] Yale-Brown Obsessive Compulsive Scale Modified for Binge Eating (YBOCS-BE) scores,[26,27] and HAM-D total scores.[24] The CGI-S is a 7-point scale on which 1 = normal, 2 = borderline ill, 3 = mildly ill, 4 = moderately ill, 5 = markedly ill, 6 = severely ill, and 7 = among the most extremely ill patients. The YBOCS-BE is a modified version of the Yale-Brown Obsessive Compulsive Scale[26] (available from the authors on request) that measures obsessiveness of binge-eating thoughts and compulsiveness of binge-eating behaviors.[27] Other secondary efficacy measures included response categories based on percentage decrease in frequency of binges from baseline to endpoint and defined as follows: remission = cessation of binges, marked = 75%–99% decrease, moderate = 50%–74% decrease, and none = less than 50% decrease. These response categories have been used in previous treatment studies of SSRIs in bulimia nervosa[14,15] and binge-eating disorder.[17–19,27]

Statistical Methods

Our data analysis procedure was almost identical to that used in a previous trial of fluoxetine in binge-eating disorder.[19] Pretreatment comparisons between assignment

Table 1. Baseline Characteristics of 38 Subjects With Binge-Eating Disorder Receiving Citalopram or Placebo[a]

Characteristic	Citalopram (N = 19)	Placebo (N = 19)
Age, mean (SD), y	42.0 (9.0)	39.2 (12.0)
Female, N (%)	18 (95)	18 (95)
White, N (%)	15 (79)	18 (95)
Current major depressive disorder, N (%)	4 (21)	8 (42)
Lifetime (current or past) major depressive disorder, N (%)	12 (63)	14 (74)

[a]Differences between groups on all characteristics were not significant.

Table 2. Baseline Measures of 38 Subjects With Binge-Eating Disorder Receiving Citalopram or Placebo, Mean (SD)[a]

Measure	Citalopram (N = 19)	Placebo (N = 19)
Binges/wk	5.2 (3.6)	5.7 (2.6)
Binge days/wk frequency	4.0 (1.7)	4.0 (1.5)
BMI, kg/m^2	41.4[b] (6.9)	34.2 (7.4)
Weight, kg	116.8[c] (21.0)	94.6 (23.2)
CGI-S score	4.5[d] (0.7)	5.0 (0.7)
YBOCS-BE score		
Total	19.4 (4.2)	18.5 (3.1)
Obsessions	9.3 (2.2)	9.3 (1.8)
Compulsions	10.1 (2.2)	9.2 (1.7)
HAM-D score	3.1 (3.2)	2.7 (3.7)

[a]Differences between groups are not significant unless noted otherwise.
[b]p = .003 vs. placebo.
[c]p = .004 vs. placebo.
[d]p = .033 vs. placebo.
Abbreviations: BMI = body mass index, CGI-S = Clinical Global Impressions-Severity of Illness scale, HAM-D = Hamilton Rating Scale for Depression, YBOCS-BE = Yale-Brown Obsessive Compulsive Scale Modified for Binge Eating.

groups were made using the Fisher exact test for categorical variables and 2-sample t tests for continuous variables.

For each outcome except response categories, we performed 2 repeated-measures random regression analyses,[28] sometimes referred to as "mixed-model repeated-measures" analyses. The first, a "time trend" analysis, was our primary analysis and compared the rate of change of each outcome measure during the treatment period between groups. We used a model for the mean of the outcome variable that included terms for treatment, time, and treatment-by-time interaction. This method is similar to that employed in 4 previous studies of binge-eating disorder[17–19,27] and described in Gibbons et al.[29] and Cnann et al.[30] We modeled time as a continuous variable, expressed as a log (weeks + 1), with weeks ranging from 0 at baseline to 6 at the week 6 visit after randomization. The logarithmic transformation was used because the response of the efficacy measures was approximately linear on the log scale, as is often found in treatment studies of psychiatric disorders.[17–19,27] The measure of effect was treatment-by-time interaction, which can be interpreted as the difference in the rate of change (change per unit of time), or the difference in slope with respect to time, of the outcome measure.

The second analysis, an "endpoint analysis," estimated the difference between groups in the change from baseline to week 6. We used a model for the mean change since baseline of the outcome measure that included terms for treatment, treatment-by-time interaction, baseline value of outcome, and baseline value-by-time interaction, as described by Mallinckrodt et al.[31] and used by Goldstein et al.[32] and Arnold et al.[19] The main difference of the endpoint from the time trend analysis is that the endpoint analysis does not assume a trend in time. It is thus less powerful if the assumption of a time trend (in this case, linear on the log scale) is correct, but represents a more conservative analysis that does not depend on this assumption.

For the analysis of binge frequency in both random regression analyses, we used the logarithmic transformation log [(binges/week) + 1] to normalize the data and stabilize the variance.

To account for the correlation of observations within individuals in the random regression analyses, we used PROC MIXED IN SAS software (SAS Institute, Cary, N.C.) to calculate the standard errors of the parameter estimates using the best-fitting of the following alternatives for the covariance matrix: compound symmetry, heterogeneous compound symmetry, first-order autoregressive, and heterogeneous first-order autoregressive.

Both random regression analyses are based on the intent-to-treat population, with the time trend analysis including available observations on all subjects who completed a baseline evaluation and the endpoint analysis including available observations on all subjects who completed at least 1 baseline evaluation. We note that both analyses account for the effects of baseline values of the outcome measures. The time trend and endpoint random regression analyses offer an improvement over endpoint analyses using completer subjects or last-observation-carried-forward analyses, in that they use available data at all points, not just endpoint data, and they make more realistic assumptions about the nature of the missing data.[29–31]

For 2 baseline measures—current major depressive disorder and BMI—we assessed whether there was a differential response in subjects by level of the measure; for example, whether subjects with current major depressive disorder or higher baseline BMI would show a greater response to treatment. To assess such effects, we first tested for an interaction between the measure and treatment for all other outcome variables. If there was no significant interaction, we further tested whether adding a term for the measure influenced the measure of effect (that is, represented a confounding variable that needed to be adjusted for in the analysis).

For the analysis of response categories, we compared differences between treatment groups using the exact trend

Table 3. Outcome Measures and Analysis of Differences Between Groups After 6 Weeks of Treatment With Citalopram or Placebo

Outcome Measure	Citalopram (N = 16) Mean (SD)	Placebo (N = 15)[a] Mean (SD)	Time Trend Analysis Difference Between Groups in Rate of Change[b] Estimate	SE	p	Endpoint Analysis Difference Between Groups in Change From Baseline to Week 6[b] Estimate	SE	p
Binges/wk	1.7 (3.1)	3.4 (3.0)	–0.311[c]	0.086	.003	–0.375[d]	0.222	.091
Binge days/wk	1.2 (2.0)	2.8 (2.2)	–0.324[e]	0.076	< .001	–0.488[f]	0.199	.016
BMI, kg/m^2	40.9 (7.0)	35.7 (7.5)	–0.525	0.145	< .001	–0.818	0.254	.001
Weight, kg	114.1 (22.4)	99.8 (24.7)	–1.43	0.40	< .001	–2.49	0.66	< .001
CGI-S score	2.4 (1.4)	3.6 (1.7)	–0.475	0.217	.028	–0.545	0.513	.29
YBOCS-BE score								
Total	7.6 (7.2)	13.2 (5.9)	–3.73	1.37	.007	–5.73	2.33	.007
Obsessions	4.3 (3.6)	6.8 (2.6)	–1.44	0.72	.046	–2.48	1.22	.041
Compulsions	3.4 (3.9)	6.4 (3.6)	–2.26	0.72	.002	–2.88	1.27	.023
HAM-D score	1.4 (2.3)	1.9 (3.1)	–1.05	0.54	.053	–2.04	0.97	.10

[a]N = 14 for BMI and weight.
[b]Random regression model includes all available observations on all subjects at all timepoints, including those who terminated the study prematurely (see text for explanation of model).
[c]Estimate and SE displayed are for log [(binges/wk) + 1] used in statistical analysis; corresponding estimate for difference between groups in rate of change from baseline (standardized at 5.5 binges/wk) to week 6 in binges/week is –1.7.
[d]Estimate and SE displayed are for log [(binges/wk) + 1] used in statistical analysis; corresponding estimate for difference between groups in change from baseline (standardized at 5.5 binges/wk) to week 6 in binges/week is –1.1.
[e]Estimate and SE displayed are for log [(binge days/wk) + 1] used in statistical analysis; corresponding estimate for difference between groups in rate of change from baseline (standardized at 4.0 binge days/wk) to week 6 in binge days/week is –1.6.
[f]Estimate and SE displayed are for log [(binge days/wk) + 1] used in statistical analysis; corresponding estimate for difference between groups in change from baseline (standardized at 4.0 binge days/wk) to week 6 in binge days/week is –1.2.
Abbreviations: BMI = body mass index, CGI-S = Clinical Global Impressions-Severity of Illness scale, HAM-D = Hamilton Rating Scale for Depression, YBOCS-BE = Yale-Brown Obsessive Compulsive Scale Modified for Binge Eating.

test for 2-by-k–ordered tables. We performed 2 analyses: one used only subjects completing the 6 weeks of treatment ("completers"), and the other was an intent-to-treat analysis using all subjects who completed at least 1 postbaseline evaluation, with the last observation carried forward.

We set alpha at .05 for statistical significance. All tests were 2-tailed.

RESULTS

Thirty-eight subjects were enrolled in the study from August 2000 through July 2001 and received randomized treatment; 19 subjects were assigned to each treatment group. An additional 12 subjects were screened but not enrolled because they failed to meet DSM-IV criteria for binge-eating disorder (N = 1), had exclusionary psychiatric diagnoses (N = 2 with bipolar disorder), withdrew consent to participate (N = 1), failed to return for the baseline visit (N = 4), or had < 3 binges in the week before randomization (N = 4). Among the 38 subjects who were enrolled, major depressive disorder was the most common co-occurring lifetime psychiatric disorder, occurring in 26 subjects (68%) as a lifetime diagnosis. It was current in 12 subjects (32%). At baseline, subjects in the 2 treatment groups were comparable with respect to age, sex, ethnicity, and current or lifetime major depressive disorder (Table 1). They were also comparable with respect to baseline values on all outcome measures, except that citalopram-treated subjects had a significantly higher mean BMI and weight and a significantly lower CGI-S score than placebo-treated subjects (Table 2).

During the course of the study, 7 subjects (3 citalopram, 4 placebo) withdrew prematurely, all after completing 4 weeks of treatment, for the following reasons: 4 for worsening depressive symptoms (1 citalopram, 3 placebo); 1 for nonadherence to the study protocol (placebo); 1 for an adverse event (citalopram—sexual dysfunction); and 1 for personal conflict (citalopram). The remaining 31 patients (16 citalopram, 15 placebo) completed the 6 weeks of treatment.

The daily dose at endpoint evaluation for citalopram-treated subjects was 60 mg for 17 subjects and 40 mg for 2 subjects (mean dose of 57.9 mg/day); the corresponding "dose" of placebo was also 60 mg for 17 subjects and 40 mg for 2 subjects.

The observed mean values for the outcome variables at week 6, by treatment group, are presented in Table 3. The time trend analysis found that the citalopram group, compared with the placebo group, had a significantly greater rate of reduction in frequency of binges (Figure 1) (p = .003), frequency of binge days (Figure 2) (p < .001), BMI (p < .001), weight (Figure 3) (p < .001), CGI-S scores (p = .028), YBOCS-BE total scores (p = .007), YBOCS-BE obsession scores (p = .046), and YBOCS-BE compulsion scores (p = .002) and a marginally significantly greater rate of reduction in HAM-D scores (p = .053) (Table 3). The endpoint analysis found that the citalopram group had a significantly greater reduction in frequency of binge days (p = .016), BMI (p = .001), and weight (p < .001) and a marginally significant reduction in frequency of binges (p = .091) and HAM-D scores (p = .10); however, the difference between groups in change in CGI-S scores was not significant (p = .29).

Figure 1. Mean Number of Binges/Week, by Treatment Group, for Subjects Remaining in the Study at Each Timepoint

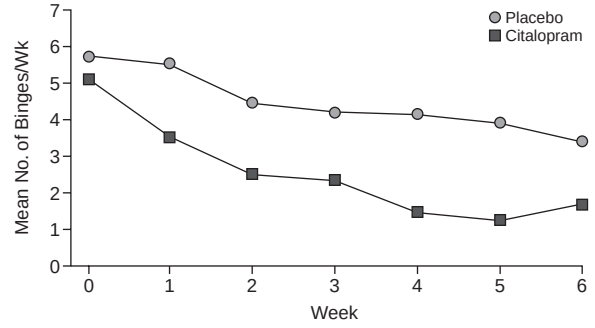


Figure 2. Mean Number of Binge Days/Week, by Treatment Group, for Subjects Remaining in the Study at Each Timepoint

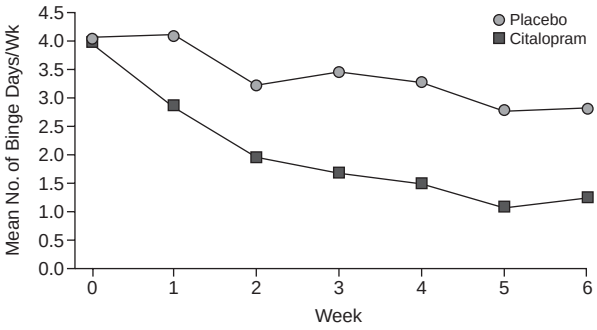
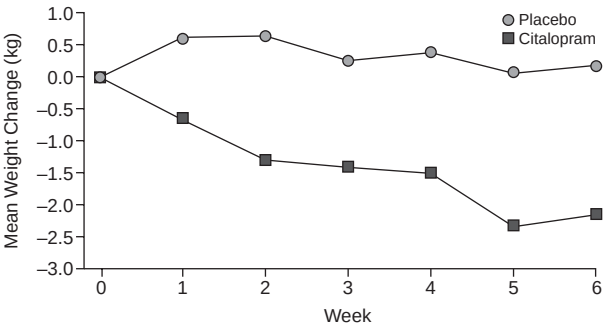


Figure 3. Mean Change in Weight (kg) From Baseline, by Treatment Group, for Subjects Remaining in the Study at Each Timepoint



The estimated mean difference in frequency of binges at week 6 (standardized to starting with 5.5 binges/week at baseline) was –1.7 from the time trend analysis and –1.1 from the endpoint analysis; the estimated mean difference in frequency of binge days at week 6 (standardized to starting with 4.0 binge days/week at baseline) was –1.6 from the time trend analysis and –1.2 from the endpoint analysis. The estimated mean difference in weight loss between groups at week 6 was –2.8 kg (–6.2 lb) from the time trend analysis and –2.5 kg (–5.6 lb) from the endpoint analysis. The observed mean difference for completers at week 6 was 2.3 kg (5.1 lb), with placebo patients gaining a mean of 0.2 kg (0.4 lb) and citalopram subjects losing a mean of 2.1 kg (4.7 lb). The correlation between weight change and percentage decrease in frequency of binges among completers was statistically significant (Spearman rank correlation: $\rho = .39$; $p = .034$).

Table 4. Response Categories for Percentage Decrease in Frequency of Binges From Baseline to Endpoint, N (%)

	Intent-to-Treat[a]		Completers[b]	
Response	Citalopram (N = 19)	Placebo (N = 19)	Citalopram (N = 16)	Placebo (N = 15)
None (< 50%)	5 (26)	11 (58)	3 (19)	7 (47)
Moderate (50%–74%)	4 (21)	3 (16)	3 (19)	3 (20)
Marked (75%–99%)	1 (5)	1 (5)	1 (6)	1 (7)
Remission (100%)	9 (47)	4 (21)	9 (56)	4 (27)

[a]Last observation carried forward; $p = .068$ for difference between groups, by exact trend test.
[b]$p = .080$ for difference between groups, by exact trend test.

For the random regression analyses, there was no evidence for differential effect in subjects with versus without current major depressive disorder, or with varying levels of baseline BMI. Additionally, adjusting for the presence of current major depressive disorder or baseline BMI did not change the estimates of the effects of treatment on any outcome variable for the time trend analysis. For the endpoint analysis, the estimated difference between groups at week 6 changed appreciably only for HAM-D score, which dropped from 2.04 to 0.67.

We also examined post hoc the effects of the 3 baseline variables—BMI, weight, and CGI-S score—that differed significantly between the treatment groups. For BMI and weight, when an analysis described above for BMI was used, there was no appreciable influence of baseline values on any outcome measure. For CGI-S, the mismatch between groups at baseline occurred largely because of differences in classification at a single level: in the placebo group, 4 were moderate and 11 were marked; in the citalopram group, 13 were moderate and 3 were marked. Because of sparse data due to the difference in covariate distribution and the narrow range of covariate values, it was not possible to test adequately for the effect of adjustment for baseline CGI-S scores on other outcome measures.

In the analysis of response categories, citalopram was associated with a higher response level than placebo, but the differences only approached statistical significance ($p = .068$ in the intent-to-treat analysis and $p = .080$ for completers, by exact trend test) (Table 4).

Table 5. Adverse Events Reported by ≥ 15% of Patients, N (%)[a]

Event	Citalopram (N = 19)	Placebo (N = 19)
Sweating	9 (47)[b]	1 (5)
Dry mouth	8 (42)	7 (37)
Headache	8 (42)	5 (26)
Diarrhea	7 (37)	4 (21)
Nausea	7 (37)	2 (11)
Sedation	5 (26)	4 (21)
Fatigue	5 (26)[c]	0 (0)
Insomnia	3 (16)	1 (5)
Sexual dysfunction	3 (16)	1 (5)

[a]Differences between groups are not significant unless noted otherwise.
[b]p = .008 vs. placebo, by Fisher exact test.
[c]p = .046 vs. placebo, by Fisher exact test.

The most common adverse events reported by the citalopram-treated subjects were sweating (N = 9), dry mouth (N = 8), headaches (N = 8), nausea (N = 7), diarrhea (N = 7), fatigue (N = 5), sedation (N = 5), insomnia (N = 3), and sexual dysfunction (N = 3) (Table 5). Except for sweating and fatigue, there were no significant differences between treatment groups in the incidence of adverse events. No serious adverse medical events were observed among the citalopram-treated subjects.

DISCUSSION

With a time trend analysis (based on the estimated difference between groups in rate of change of outcome measures) as the primary efficacy analysis, citalopram treatment of binge-eating disorder was associated with a significantly greater reduction than placebo treatment in frequency of binges, frequency of binge days, BMI, weight, obsessive-compulsive features of binge-eating symptoms, and severity of illness, as well as a marginally significant reduction in depression rating scale scores. With a more conservative endpoint analysis (based on the estimated difference between groups in the change from baseline to week 6), citalopram treatment was associated with a significantly greater reduction than placebo in frequency of binge days, BMI, and weight, but the differences in change in frequency of binges and in reduction of depression rating scale scores only approached statistical significance. There was greater improvement in response categories in the citalopram compared with the placebo group, but this difference was only marginally significant. Taken together, these findings provide preliminary evidence for clinically important effects of citalopram on binge frequency, obsessive-compulsive features of binge eating, severity of illness, and weight in binge-eating disorder. In addition, citalopram was generally well tolerated and associated only with known side effects of the medication.

The decreased frequency of binges, reduced severity of illness, and weight loss associated with citalopram in this trial are consistent with the 3 previous controlled trials of other SSRIs—fluvoxamine,[17] sertraline,[18] and fluoxetine[19]—in the treatment of binge-eating disorder. The correlation between weight change and percentage decrease in frequency of binges among those who completed 6 weeks of randomized treatment was statistically significant—similar to results in 2 of the other studies of SSRIs in binge-eating disorder.[17,19] Reduction of binge-eating episodes through treatment with citalopram and other SSRIs may lead to weight loss through a decrease in energy intake.

The mechanism of action of citalopram in the treatment of binge-eating disorder is unknown. Side effects such as abdominal bloating (N = 0, citalopram; N = 2, placebo), abdominal cramps (N = 1, citalopram; N = 2, placebo), dyspepsia (N = 1, citalopram; N = 0, placebo), nausea (N = 7, citalopram; N = 2, placebo), taste perversion (N = 0, citalopram; N = 1, placebo), and vomiting (N = 0, citalopram; N = 2, placebo) may have reduced binge eating; however, in this study, the citalopram and placebo groups did not differ in the incidence of these side effects. Citalopram, as an SSRI, may correct an abnormality of serotonin neurotransmission. Although there are limited studies of serotonin neurotransmission in binge-eating disorder,[33] there is considerable evidence of dysfunction of serotonergic processes in patients with bulimia nervosa,[34] a condition related to binge-eating disorder.[2] Further support for serotonergic dysfunction occurring in binge-eating disorder comes from a positive placebo-controlled study of *d*-fenfluramine, a serotonin-releasing agent, in the treatment of binge-eating disorder.[35] However, this medication has been withdrawn from the market because of safety concerns. Of note, we found that almost all of the subjects with binge-eating disorder in our study required the full 60 mg/day of citalopram to achieve an adequate response, with only 2 subjects taking less than that amount at endpoint.

Several limitations of this study should be considered. First, because the duration of treatment was only 6 weeks, the results may not generalize to longer treatment periods. Future studies should address the long-term efficacy of citalopram and other SSRIs in binge-eating disorder. Second, the size of the groups was relatively small. Therefore, the confidence intervals for the treatment effects are wide, and the data are compatible with a large range of effects. Third, the 2 groups were not identical at baseline. Specifically, the citalopram group had a significantly higher baseline mean body weight and BMI, but a significantly lower mean CGI-S score. This most likely occurred because we randomly assigned subjects to treatment without stratifying for weight, BMI, or global severity of illness and the sample size was relatively small. Fourth, individuals with several forms of psychopathology were excluded. Thus, the results may not generalize to binge-eating disorder with certain forms of comorbid psycho-

pathology, such as bipolar disorder. We also had limited power to detect any potential differential effects of treatment in subjects with and without concomitant disorders, such as major depressive disorder and anxiety disorders. Fifth, because the majority of subjects were female, it is unknown if these results would extend to males.

In summary, in a 6-week, randomized, placebo-controlled, flexible-dose trial, citalopram was found to be well tolerated and efficacious in reducing binge frequency, weight, and severity of illness in subjects with binge-eating disorder. In light of the study's limitations, however, these findings should be considered preliminary and in need of replication in larger, longer-term trials with a broader range of subjects with binge-eating disorder.

Drug names: citalopram (Celexa), fluoxetine (Prozac and others), fluvoxamine (Luvox and others), sertraline (Zoloft).

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