A Placebo-Controlled, Randomized Trial of Fluoxetine in the Treatment of Binge-Eating Disorder

Lesley M. Arnold, M.D.; Susan L. McElroy, M.D.; James I. Hudson, M.D., Sc.D.; Jeffrey A. Welge, Ph.D.; Aurora J. Bennett, M.D.; and Paul E. Keck, Jr., M.D.

Background: The purpose of this study was to assess the efficacy and safety of fluoxetine in the treatment of binge-eating disorder.

Method: Sixty outpatients with a DSM-IV diagnosis of binge-eating disorder were randomly assigned to receive either fluoxetine, 20 to 80 mg/day (N = 30), or placebo (N = 30) in a 6-week, double-blind, flexible-dose study. The primary measure of efficacy was frequency of binge eating. Secondary measures included body mass index, weight, Clinical Global Impressions-Severity of Illness score, Hamilton Rating Scale for Depression (HAM-D) score, and response categories. The outcome measures were analyzed using 2 random regression methods, 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 fluoxetine (mean ± SD endpoint dose = 71.3 ± 11.4 mg/day) had a significantly greater reduction in frequency of binge eating ($p = .033$), body mass index ($p < .0001$), weight ($p = .001$), and severity of illness ($p = .032$) and a marginally significant reduction in HAM-D scores ($p = .061$). Differences between groups on response categories were not statistically significant.

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

(J Clin Psychiatry 2002;63:1028–1033)

Received Dec. 12, 2001; accepted May 3, 2002. From the Women's Health Research Program (Drs. Arnold and Bennett) and the Biological Psychiatry Program (Drs. McElroy, Welge, and Keck), Department of Psychiatry, University of Cincinnati Medical Center, Cincinnati, Ohio; the Biological Psychiatry Laboratory, McLean Hospital, Belmont, Mass. (Dr. Hudson); the Department of Psychiatry, Harvard Medical School (Dr. Hudson); and the Departments of Biostatistics and Epidemiology, Harvard School of Public Health, Cambridge, Mass. (Dr. Hudson).

Supported by an investigator-initiated grant from Eli Lilly and Company, Indianapolis, Ind. (Dr. Arnold).

Dr. McElroy has been a consultant for Abbott, Elan, Lilly, Glaxo Wellcome, Janssen, Ortho-McNeil, and Parke-Davis; has been on the speakers/advisory board for Abbott, Lilly, Glaxo Wellcome, Janssen, Ortho-McNeil, Parke-Davis, and Solvay; and has received grant support from Abbott, Lilly, Forest, Glaxo Wellcome, Ortho-McNeil, Parke-Davis, Pfizer, Sanofi-Synthelabo, and Solvay.

Corresponding author and reprints: Lesley M. Arnold, M.D., University of Cincinnati Medical Center, 231 Albert B. Sabin Way, P.O. Box 670559, Cincinnati, OH 45267-0559 (e-mail: Lesley.Arnold@uc.edu).

Binge-eating disorder is characterized by recurrent binge-eating episodes in which large amounts of food are consumed in a discrete period of time and there is a sense of lack of control over eating during the episode.[1] Several studies have found that approximately 30% of individuals attending weight loss programs have binge-eating disorder.[2,3] The current prevalence of binge-eating disorder in the general population of the United States is estimated to be 2% to 5%.[2,3] Binge-eating disorder is frequently associated with obesity and psychiatric comorbidity, most commonly major depressive disorder.[2,4–6]

Binge eating is a major feature of bulimia nervosa, but binge-eating disorder differs from bulimia nervosa in that self-induced vomiting, misuse of laxatives, or other types of inappropriate compensatory behavior to prevent weight gain do not follow binges.[1] Bulimia nervosa responds to treatment with a wide range of antidepressants, including selective serotonin reuptake inhibitors (SSRIs).[6,7] Placebo-controlled studies have demonstrated a significant therapeutic effect of fluoxetine, which is indicated for the treatment of bulimia nervosa.[8,9]

Although binge-eating disorder has no established psychopharmacologic treatment, antidepressants have been recently studied in controlled trials in patients with binge-eating disorder, in part because of the phenomenological similarities between bulimia nervosa and binge-

eating disorder and the favorable response of bulimia nervosa to antidepressants.[6] Two recent studies found fluvoxamine[10] and sertraline[11] to be superior to placebo in the treatment of binge-eating disorder. On the basis of this evidence and the efficacy of fluoxetine in bulimia nervosa, we conducted a placebo-controlled, randomized trial to assess the efficacy and safety of fluoxetine in 60 outpatients with 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 fluoxetine or placebo for a 6-week treatment period. All medications were dispensed in identical capsules (20 mg of fluoxetine or placebo). Subjects began randomized treatment with 20 mg/day for the first 3 days. The dosage was then increased, as tolerated, to 40 mg/day for 3 days and then to 60 mg/day. After 2 weeks of treatment with 60 mg/day, the dose could be increased to 80 mg/day. Adjustments within the range of 1 capsule per day to 4 capsules per day were at the discretion of the investigators (all of whom were blinded to treatment assignment) and were made until a subject improved or intolerance intervened.

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 and also had experienced ≥ 3 binge-eating episodes weekly for at least 6 months. Subjects were between 18 and 60 years of age and weighed more than 85% of their ideal body weight.[12] Subjects were excluded if they were pregnant or lactating; had concurrent anorexia nervosa, concurrent or recent (within 1 year of study entry) substance abuse or dependence, or 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 to 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 fluoxetine; 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 protocol that included the following assessments and procedures: an interview for demographic information and medical, psychiatric, and family histories; the Structured Clinical Interview for DSM-IV (SCID)[13]; physical examination; vital signs; height and weight; and routine blood chemical and hematologic tests. Subjects were given diaries at this and each of the following visits 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 screening visit, subjects were assessed for number of binges experienced since the last visit, Clinical Global Impressions-Severity of Illness (CGI-S)[14] rating (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), medication dose, medication compliance ascertained by capsule count, adverse events, use of nonstudy medications, vital signs, and weight. We administered the 17-item Hamilton Rating Scale for Depression (HAM-D)[15] at baseline and weeks 2, 4, and 6.

Outcome Measures

The primary outcome measure was the weekly frequency of eating binges. Secondary outcome measures were weight, body mass index (BMI; body weight in kg divided by height in m^2), CGI-S score, HAM-D total score, and response categories based on percentage decrease in frequency of binges from baseline to endpoint as follows: remission = cessation of binges, marked = 75% to 99% decrease, moderate = 50% to 74% decrease, and none = less than 50% decrease. These response categories have been used in previous treatment studies of SSRIs in bulimia nervosa[8,9] and binge-eating disorder.[10,11]

Statistical Methods

Pretreatment comparisons between assignment 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,[16] 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 2 previous studies of binge-eating

Table 1. Baseline Characteristics of 60 Subjects With Binge-Eating Disorder Receiving Fluoxetine or Placebo[a]

Characteristic	Fluoxetine (N = 30)	Placebo (N = 30)
Age, mean ± SD, y	41.9 ± 9.7	40.8 ± 9.0
Female	28 (93)	28 (93)
White	27 (90)	26 (87)
African American	3 (10)	4 (13)
Duration of binge-eating disorder, mean ± SD, y[b]	19.9 ± 12.5	16.7 ± 9.5
Current major depressive disorder	8 (27)	7 (23)
Lifetime (current or past) major depressive disorder	20 (67)	19 (63)

[a]Values shown as N (%) unless otherwise noted. There were no statistically significant differences between the treatment groups.
[b]Fluoxetine N = 27, placebo N = 29.

Table 2. Baseline Measurements (mean ± SD) of 60 Subjects With Binge-Eating Disorder Receiving Fluoxetine or Placebo[a]

Measure	Fluoxetine (N = 30)	Placebo (N = 30)
No. of binges/week[b]	6.0 ± 2.5	6.1 ± 4.8
Weight, kg[c]	110.4 ± 24.1	103.5 ± 19.0
Body mass index[c]	39.6 ± 7.0	36.7 ± 6.8
CGI-S score	4.2 ± 0.4	4.3 ± 0.6
HAM-D score	4.8 ± 4.3	4.2 ± 2.9

[a]There were no statistically significant differences among the treatment groups. Abbreviations: CGI-S = Clinical Global Impressions-Severity of Illness scale, HAM-D = Hamilton Rating Scale for Depression.
[b]Placebo N = 29.
[c]Fluoxetine N = 29.

disorder[10,11] and described in Gibbons et al.[17] and Cnaan et al.[18] 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.[10,11,17] 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 from baseline in 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.[19] and used by Goldstein et al.[20] The main difference of the endpoint analysis 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 transformations 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 intent-to-treat, 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 last 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 subjects who completed the study or last-observation-carried-forward (LOCF) 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.[17–19]

To assess whether there was a differential response in subjects with and without current major depressive disorder, we tested for an interaction between current major depressive disorder and treatment. If there was no significant interaction, we further tested whether adding a term for current major depressive disorder 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 test for 2-by-k–ordered tables. We performed 2 analyses: one including only subjects who completed 6 weeks of treatment ("completers"), and the other, an intent-to-treat analysis, including all subjects who completed at least 1 postbaseline evaluation, using LOCF.

RESULTS

Sixty subjects were enrolled in the study from February 1998 to June 2000 and received randomized treatment; 30 subjects were assigned to each treatment group. Major depressive disorder, the most common comorbid lifetime Axis I psychiatric diagnosis, occurred in 39 subjects (65%) as a lifetime diagnosis and was current in 15 subjects (25%). At baseline, subjects in the 2 treatment groups were comparable with respect to age, sex, ethnicity, duration of binge-eating disorder, and current or lifetime major depressive disorder (Table 1). They were also comparable with respect to baseline values of all outcome measures (Table 2).

Table 3. Outcome Measures and Analysis of Differences Between Groups After 6 Weeks of Treatment With Fluoxetine or Placebo[a]

	Week 6 Values (mean ± SD)							
	Fluoxetine	Placebo	Time Trend Analysis[d]			Endpoint Analysis[e]		
Outcome Measure	(N = 23)[b]	(N = 13)[c]	Estimate	SE	p	Estimate	SE	p
No. of binges/week	1.8 ± 2.9	2.7 ± 3.8	–0.251[f]	0.118	.033	–0.311[g]	0.256	.22
Body mass index, kg/m^2	40.0 ± 7.2	39.5 ± 6.3	–0.484	0.110	< .0001	–1.41	0.26	< .0001
Weight, kg	112.5 ± 25.0	110.3 ± 18.2	–1.21	0.37	.001	–3.59	0.77	< .0001
CGI-S score	2.2 ± 1.4	3.3 ± 1.4	–0.375	0.175	.032	–1.02	0.40	.012
HAM-D score	2.6 ± 3.0	5.5 ± 4.1	–1.09	0.58	.061	–3.01	1.02	.003

[a]Abbreviations: CGI-S = Clinical Global Impressions-Severity of Illness scale, HAM-D = Hamilton Rating Scale for Depression.
[b]N = 12 for binges/week.
[c]N = 22 for weight.
[d]Time trend analysis shows the difference between groups in rate of change. Random regression model includes all available observations on all subjects at all timepoints (N = 30 for both groups), including those who terminated the study prematurely (see text for explanation of model).
[e]Endpoint analysis shows the difference between groups in change from baseline to week 6. Random regression model includes observations on subjects who completed at least 1 baseline evaluation (N = 29 for fluoxetine, N = 21 for placebo), including those who terminated the study prematurely (see text for explanation of model).
[f]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 6 binges/week) to week 6 in binges/week is –1.1.
[g]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 6 binges/week) to week 6 in binges/week is –0.7.

During the course of the study, 24 subjects withdrew; 17 from the placebo group and 7 from the fluoxetine group. The reasons for withdrawal were as follows: lost to follow-up (fluoxetine group N = 3, placebo group N = 10); an adverse medical event (fluoxetine group N = 2, placebo group N = 2), including sedation, hand and foot swelling, palpitations, diarrhea, nausea, and apathy; lack of efficacy (fluoxetine group N = 0, placebo group N = 2); and other non–drug-related reasons (fluoxetine group N = 2, placebo group N = 3). A significantly greater proportion of placebo-treated subjects than fluoxetine subjects withdrew from the study (N = 17 placebo-treated subjects [57%] vs. N = 7 fluoxetine-treated subjects [23%]; p = .02, Fisher exact test). More placebo-treated subjects than fluoxetine-treated subjects were lost to follow-up, and this difference approached statistical significance (p = .06, Fisher exact test). The proportion of dropouts was similar among subjects with and without current major depressive disorder (5 [33%] of 15 depressed subjects vs. 20 [44%] of 45 nondepressed subjects; p = .55).

Endpoint data for the endpoint random regression analysis and the intent-to-treat analysis of the response categories were not available for 10 of the subjects who withdrew (9 from the placebo group and 1 from the fluoxetine group), because they dropped out before a single postbaseline visit. The reason for the differential dropout rate is unclear. We do not have evidence that rapid response to fluoxetine was a cause for this phenomenon. Eight of the 10 subjects were lost to follow-up, 1 from the placebo group dropped out because the study required too much time, and another from the placebo group dropped out because of side effects.

The mean ± SD dose at endpoint evaluation for fluoxetine-treated subjects was 71.3 ± 11.4 mg/day. The corresponding mean "dose" of placebo (based on the number of capsules given) was 67.3 ± 11.5 mg/day.

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 fluoxetine group, compared with the placebo group, had a significantly greater reduction in frequency of binges (p = .033), BMI (p < .0001), weight (p = .001), and CGI-S scores (p = .032) and a marginally significantly greater reduction in HAM-D scores (p = .061) (Table 3). The endpoint analysis found that the fluoxetine group had a significantly greater reduction in BMI (p < .0001), weight (p < .0001), CGI-S scores (p = .012), and HAM-D scores (p = .003); however, the difference between groups in change in frequency of binges was not significant (p = .22).

The estimated mean difference between groups in frequency of binges at week 6 (standardized to starting with 6 binges/week at baseline) was 1.1 from the time trend analysis and 0.7 from the endpoint analysis; the corresponding observed mean difference among those completing 6 weeks of treatment was 0.7. The estimated mean difference in weight loss between groups at week 6 was 2.4 kg (5.3 lb) from the time trend analysis and 3.6 kg (8.0 lb) from the endpoint analysis. The observed mean difference for completers at week 6 was 3.9 kg (8.7 lb), with placebo patients gaining a mean of 0.7 kg (1.6 lb) and fluoxetine subjects losing a mean of 3.3 kg (7.3 lb). The correlation between weight change and percentage decrease in frequency of binges among completers approached statistical significance (Spearman rank correlation: r = 0.30; p = .097).

For the random regression analyses, there was no evidence for differential effect in subjects with versus without current major depressive disorder. Also, adjusting for the presence of current major depressive disorder did not change the estimates of the effects of treatment on any outcome variable.

Table 4. Response Categories for Percentage Decrease in Binges/Week From Baseline to Endpoint[a]

	Intent-to-Treat[b]		Completers[c]	
Response Category	Fluoxetine (N = 29)	Placebo (N = 21)	Fluoxetine (N = 23)	Placebo (N = 12)[d]
None (< 50%)	7 (24)	9 (43)	4 (17)	4 (33)
Moderate (50%–74%)	8 (28)	4 (19)	5 (22)	2 (17)
Marked (75%–99%)	1 (3)	3 (14)	1 (4)	3 (25)
Remission (100%)	13 (45)	5 (24)	13 (57)	3 (25)

[a]Values shown as N (%).
[b]Last observation carried forward; p = .18 for difference between groups, by exact trend test.
[c]p = .21 for difference between groups, by exact trend test.
[d]Data missing from 1 placebo completer.

In the analysis of response categories, fluoxetine was associated with a higher response level than placebo, but the differences did not reach statistical significance (p = .21 for completers and p = .18 in the intent-to-treat analysis, by exact trend test) (Table 4).

The most common adverse events reported by the fluoxetine-treated subjects were dry mouth (N = 11), headache (N = 9), nausea (N = 7), insomnia (N = 7), diarrhea (N = 6), fatigue (N = 6), sedation (N = 5), increased urinary frequency (N = 4), and sexual dysfunction (N = 4). There were no significant differences between treatment groups in the incidence of adverse events.

DISCUSSION

Using a time trend analysis (based on the estimated difference between groups in rate of change of outcome measures) as the primary efficacy analysis, we found that fluoxetine treatment of binge-eating disorder was associated with a significantly greater reduction than placebo treatment in frequency of binges, BMI, weight, and severity of illness, as well as a marginally significant reduction in depression rating scale scores. When a more conservative endpoint analysis (based on the estimated difference between groups in the change from baseline to week 6) was used, fluoxetine treatment was associated with a significantly greater reduction than placebo in BMI, weight, severity of illness, and depression rating scale scores, but the difference in change in frequency of binges was not significant. There was greater improvement in response categories in the fluoxetine compared with the placebo group, but this difference was not statistically significant. Taken together, these findings provide some evidence for clinically important effects of fluoxetine on frequency of binges and depression rating scale scores and more consistent evidence for effects on weight and severity of illness. Fluoxetine treatment was generally well tolerated and associated with only known side effects of this medication.

The results of this trial, which show decreased frequency of binges and severity of illness associated with fluoxetine, are consistent with those of 2 previous controlled trials of other SSRIs, fluvoxamine[10] and sertraline,[11] in the treatment of binge-eating disorder. As in previous placebo-controlled studies of binge-eating disorder,[10,11] there was a high placebo response: at last observation, 57% of placebo-treated subjects had at least a 50% reduction in binges/week.

Consistent with the other controlled studies of SSRIs in the treatment of binge-eating disorder,[10,11] fluoxetine was associated with significant weight loss. After 6 weeks of fluoxetine treatment, subjects lost a mean of 3.3 kg (7.3 lb). The correlation between weight change and percentage decrease in frequency of binges among those who completed 6 weeks of randomized treatment approached statistical significance. In the study of fluvoxamine in binge-eating disorder, the decreases in BMI and in the frequency of binges were significantly correlated in those who completed the study.[10] Reduction of binge-eating episodes through treatment with fluoxetine and other SSRIs may lead to weight loss through a decrease in energy intake.

The mechanism of action of fluoxetine in the treatment of binge-eating disorder is unknown. Side effects such as anorexia, dyspepsia, and nausea may have reduced binge eating; however, in this study, the fluoxetine and placebo groups did not differ in the incidence of these side effects. Fluoxetine, as an SSRI, may correct an abnormality of serotonin neurotransmission. Although there are limited studies of abnormalities of serotonin neurotransmission in binge-eating disorder,[21] there is considerable evidence of dysfunction of serotonergic processes in patients with bulimia nervosa,[22] a condition related to binge-eating disorder.[6] As in the treatment of bulimia nervosa, in which fluoxetine at 60 mg/day seems to be required for an optimal response,[8] we found that most of the subjects with binge-eating disorder in our study required 60 to 80 mg/day of fluoxetine to achieve an adequate response, with the mean ± SD final dose being 71.3 ± 11.4 mg/day.

In addition to SSRIs, several other pharmacologic treatments for binge-eating disorder have been proposed. There is evidence from open-label studies for the efficacy of sibutramine[23] and venlafaxine,[24] as well as evidence from an open-label[25] and a randomized placebo-controlled study[26] for efficacy of topiramate. Another drug found to be superior to placebo in the treatment of binge-eating disorder, *d*-fenfluramine,[27] has been withdrawn from the market because of safety concerns.

Several limitations of this study should be considered. First, because the duration of treatment was 6 weeks, the results may not generalize to longer treatment periods. Future studies should address the long-term efficacy of fluoxetine. Second, individuals with several forms of lifetime psychopathology were excluded. Thus, the results may not generalize to individuals with certain forms of comorbid psychopathology 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 disorder. Third, 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.

In summary, in a 6-week, randomized, placebo-controlled, flexible-dose trial, fluoxetine was found to be well tolerated and effective in reducing binge frequency, weight, and severity of illness in subjects with binge-eating disorder.

Drug names: fluoxetine (Prozac and others), fluvoxamine (Luvox and others), sertraline (Zoloft), sibutramine (Meridia), topiramate (Topamax), venlafaxine (Effexor).

REFERENCES

1. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition. Washington, DC: American Psychiatric Association; 1994
2. Spitzer RL, Devlin M, Walsh BT, et al. Binge eating disorder: a multisite field trial of the diagnostic criteria. Int J Eat Disord 1992;11:191–203
3. Spitzer RL, Yanovski S, Wadden T, et al. Binge eating disorder: its further validation in a multisite study. Int J Eat Disord 1993;13:137–153
4. Yanovski SZ, Nelson JE, Dubbert BK, et al. Association of binge eating disorder and psychiatric comorbidity in obese subjects. Am J Psychiatry 1993;150:1472–1479
5. de Zwaan M, Mitchell JE, Raymond NC, et al. Binge eating disorder: clinical features and treatment of a new diagnosis. Harv Rev Psychiatry 1994;1:310–325
6. Hudson JI, Carter WP, Pope HG Jr. Antidepressant treatment of binge-eating disorder: research findings and clinical guidelines. J Clin Psychiatry 1996;57(suppl 8):73–79
7. Hudson JI, Pope HG Jr, Carter WP. Pharmacologic therapy of bulimia nervosa. In: Goldstein D, ed. The Management of Eating Disorders and Obesity. Totowa, NJ: Humana Press, Inc; 1999:19–32
8. Fluoxetine Bulimia Nervosa Collaborative Study Group. Fluoxetine in the treatment of bulimia nervosa: a multicenter, placebo-controlled, double-blind trial. Arch Gen Psychiatry 1992;49:139–147
9. Goldstein DJ, Wilson MG, Thompson VL, et al, and the Fluoxetine Bulimia Nervosa Research Group. Long-term fluoxetine treatment of bulimia nervosa. Br J Psychiatry 1995;166:660–666
10. Hudson JI, McElroy SL, Raymond NC, et al. Fluvoxamine in the treatment of binge-eating disorder: a multicenter, placebo-controlled, double-blind trial. Am J Psychiatry 1998;155:1756–1762
11. McElroy SL, Casuto LS, Nelson EB, et al. Placebo-controlled trial of sertraline in the treatment of binge eating disorder. Am J Psychiatry 2000;157:1004–1006
12. Metropolitan Life Insurance Company. 1983 Metropolitan height and weight tables. Stat Bull Metrop Life Found 1983;64:3–9
13. First MB, Spitzer RL, Gibbon M, et al. Structured Clinical Interview for the DSM-IV Axis I Disorders-Patient Edition (SCID-I/P, Version 2.0). New York, NY: Biometric Research, New York State Psychiatric Institute; 1995
14. Guy W. ECDEU Assessment Manual for Psychopharmacology. US dept Health, Education, and Welfare publication (ADM) 76-338. Rockville, Md: National Institute of Mental Health; 1976:218–222
15. Hamilton M. A rating scale for depression. J Neurol Neurosurg Psychiatry 1960;23:56–62
16. Diggle PJ, Liang K, Zeger SL. Analysis of Longitudinal Data. Oxford, UK: Oxford University Press; 1995
17. Gibbons RD, Hedeker D, Elkin I, et al. Some conceptual and statistical issues in analysis of longitudinal psychiatric data. Arch Gen Psychiatry 1993;50:739–750
18. Cnaan A, Laird NM, Slasor P. Using the general linear mixed model to analyse unbalanced repeated measures and longitudinal data. Stat Med 1997;16:2349–2380
19. Mallinckrodt CH, Clark WS, David SR. Accounting for dropout bias using mixed-effects models. J Biopharm Stat 2001;11:9–21
20. Goldstein DJ, Mallinckrodt C, Lu Y, et al. Duloxetine in the treatment of major depressive disorder: a double-blind clinical trial. J Clin Psychiatry 2002;63:225–231
21. Monteleone P, Brambilla F, Bortolotti F, et al. Serotonergic dysfunction across the eating disorders: relationship to eating behaviour, purging behaviour, nutritional status and general psychopathology. Psychol Med 2000;30:1099–1110
22. Kaye W, Gendall K, Strober M. Serotonin neuronal function and selective serotonin reuptake inhibitor treatment in anorexia and bulimia nervosa. Biol Psychiatry 1998;44:825–838
23. Appolinario JC, Godoy-Matos A, Fontenelle LF, et al. An open-label trial of sibutramine in obese patients with binge-eating disorder. J Clin Psychiatry 2002;63:28–30
24. Malhotra S, King KH, Welge JA, et al. Venlafaxine treatment of binge-eating disorder associated with obesity: a series of 35 patients. J Clin Psychiatry 2002;63:802–806
25. Shapira NA, Goldsmith TD, McElroy SL. Treatment of binge-eating disorder with topiramate: a clinical case series. J Clin Psychiatry 2000;61:368–372
26. McElroy SL, Arnold LM, Shapira NA, et al. Topiramate in the treatment of binge eating disorder associated with obesity. Presented at the 53rd annual meeting of the American Psychiatric Association Institute on Psychiatric Services; Oct 10–14, 2001; Orlando, Fla
27. Stunkard A, Berkowitz R, Tanrikut C, et al. d-Fenfluramine treatment of binge eating disorder. Am J Psychiatry 1996;153:1455–1459