Open Trial of Fluvoxamine in the Treatment of Bulimia Nervosa

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Twenty patients suffering from bulimia nervosa received 50–150 mg fluvoxamine daily for a period of 8 weeks. Primary end-points included the Eating Disorders Inventory (EDI), the Severity Index of Bulimic Condition (BINGE), Clinical Global Impression (CGI) scores, and the number of binge eating episodes per week. Other variables assessed included the 17-item Hamilton Depression Scale and adverse experience checklist. Compared with baseline, total EDI scores increased significantly from 137.8 to 155.3 after 8 weeks of fluvoxamine treatment ($p < .001$); CGI score fell significantly from 3.5 to 2.3 ($p < .01$) during this period. The mean number of binge eating episodes recorded by patients significantly decreased ($p < .001$). Further significant improvements in bulimic behavior were noted using the BINGE questionnaire. Nine of 20 patients complained of adverse experiences, all of which were mild; the most common symptoms were somnolence ($n = 4$) and insomnia ($n = 3$). Fluvoxamine appears to be a safe and effective treatment for bulimia nervosa.

Experimental and pharmacological evidence support the hypothesis that disturbances in brain serotonin (5-HT) function play an important role in the pathophysiology of bulimia nervosa. Patients with bulimia nervosa, regardless of the presence of anorexia nervosa or major depression, have significantly blunted prolactin responses to the 5-HT agonist, meta-chlorophenyl-piperazine (Brewerton, Brandt, Lessem, Murphy, & Jimerson, 1990). In addition, the severity of bulimic symptoms has been correlated with the lowering of 5-hydroxyindoleacetic acid in the cerebrospinal fluid, also pointing to an alteration of 5-HT function (Jimerson, Lesem, Kaye, & Brewerton, 1988). The clinical response to

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several psychotropic agents known to potentiate 5-HT further supports the notion of a 5-HT dysregulation in bulimia nervosa.

The present open-label trial is designed to measure the efficacy of fluvoxamine, a potent and selective 5-HT reuptake inhibitor, in the treatment of bulimia nervosa.

METHODS

Patients

Twenty consecutive referrals of outpatient bulimics were treated with a rising-dose schedule of fluvoxamine for 8 weeks. Patients aged between 18 and 60 years were included in the study if they met the DSM-III-R criteria for bulimia nervosa, and had a total score on the 17-item Hamilton Depression Scale (HAM-D) below 15.

Patients were excluded if their current weight was more than 25% above their ideal weight, if they had clinically significant medical illness, history of major depressive episodes, abnormal plasma potassium levels, or taken anorectic or psychoactive medication in the preceding 2 weeks.

Medication

Following a washout period of 1 week (no placebo tablets were administered), patients received 50 mg fluvoxamine daily for 1 week, 100 mg/day during the second week, and 150 mg/day in subsequent weeks. All medication was taken in a single dose after the evening meal. The investigator allowed the use of lorazepan (3 mg/day) when necessary. No psychotherapy was carried out during the study. Informed consent was obtained from all patients.

End-Points

All variables were evaluated by a psychiatrist (M.P.) at weekly intervals during the first 3 weeks, then every 2 weeks until the end of the trial. Baseline data for all the assessments were compared with those at Weeks 1 and 2, and the end of treatment.

The primary efficacy variables were Eating Disorders Inventory (EDI), Severity Index of Bulimic Condition (BINGE), and Clinical Global Impression (CGI) scores together with the number of binge episodes per week recorded in the patients' diaries. The BINGE scale uses the following definitions—frequency of binges: none, infrequent (less than two per week), frequent (three to six per week), and daily; quality of life categories: poor, moderate, good, or very good; and for other variables: absent, mild, moderate, or severe.

Other variables measured included the HAM-D (17-item) rating scale and adverse experiences (DOTES) checklist.

Measurements of blood pressure, pulse rate, and body weight were also recorded. Routine hematological and biochemical tests and echocardiograms (ECGs) were performed at baseline and the end of the study.

Statistics

The following statistical tests were performed: paired t test of paired variance analysis for quantitative variables; Wilcoxon or Friedman test for non-Gaussian distribution; and the McNemar test for qualitative variables.

RESULTS

Seventeen female and three male patients aged 20 to 47 years (mean: 34.0 years) entered the study. Patients had been suffering from bulimia for a mean of 7.9 years (range 3 to 16 years). Demographic and clinical data at baseline are given in Table 1. Of the 20 patients admitted, 1 withdrew after 7 weeks of treatment, complaining of persistent insomnia throughout the active treatment period. All patients were included in the end-point evaluation.

Primary Variables

The mean total EDI scores increased from 137.8 at baseline to 143.0 at the end of the second week ($p < .05$), and to 155.3 at the end of the trial ($p < .001$). The analysis of data corresponding to the BINGE questionnaire showed statistically significant differences for the items: frequency of binges, laxative abuse, abnormal diet, dietary restriction, and influence on the quality of life. The remaining items (body shape and body weight) were not significantly changed. CGI score showed a decrease from 3.5 at baseline to 2.3 at the end of the study ($p < .01$). The mean number of binge eating episodes was calculated at baseline and at Weeks 1, 2, and 8 from data recorded by patients every week in their diaries (Table 2). There was a statistically significant decrease in binge eating episodes at each of the three assessments. Compared with baseline, a significant difference ($p < .01$) was observed as early as the first week of treatment.

Secondary Variables

The mean HAM-D (17-item) total score decreased from 8.5 at baseline to 2.2 at end-point ($p < .01$), but this was not clinically significant. Nine of the 20 patients (45.5%) complained of some adverse experiences during treatment. All adverse experiences were rated as mild. The most frequently reported symptoms were somnolence (4 cases) and insomnia (3 cases). Nausea, a side effect frequently reported in other studies with fluvoxamine, was only mentioned on two occasions. Two patients complained of headache, and one patient reported diarrhea in the first week of treatment.

Table 1. Demographic and clinical data at baseline

Sex	17 female 3 male	
Marital status		
Single	8	
Married	10	
Widowed	1	
Divorced	1	
	M	*SD*
Age	34.0	13.7
Age of onset of bulimia	22.4	10.0
Duration of present episode (months)	6.8	2.2
Pretreatment weight (kg)	76.8	16.7
Height (cm)	164.6	9.9
Pretreatment Hamilton Depression Scale score	8.5	2.2
Pretreatment Clinical Global Impression score	3.4	1.0

Table 2. Mean number of binge eating attacks

Assessment	Number
Baseline	5.5 ± 2.7
Week 1	4 ± 1.9
Week 2	2.4 ± 1.6
Week 8	1.4 ± 1.1

Fluvoxamine had no clinically relevant effect on arterial blood pressure and pulse rate. No abnormalities were found in the laboratory tests and ECGs. A significant decrease in patients' body weight was observed over the treatment period (mean loss: 3.8 kg, $p < .01$).

DISCUSSION

The results indicate that fluvoxamine improves bulimic symptoms as shown by the significant increase in the mean total EDI scores at Weeks 2 and 8, and by the significant reduction in the CGI score at Week 8. Five of the seven items in the BINGE questionnaire showed significant improvements following fluvoxamine treatment and the mean number of binge eating episodes calculated from the patients' diaries showed significant reductions over the 8-week trial. Significant improvements in the majority of the primary efficacy variables were recorded at the Week 2 assessment and suggest that the speed of onset of fluvoxamine's therapeutic effect in bulimia nervosa is rapid. The HAM-D total score also improved significantly but did not seem to be related to global improvement in bulimic behavior because the rating scores belonged to the low end of the scale.

Fluvoxamine was well tolerated and the reported adverse experiences were rated as mild. Only one patient withdrew after 7 weeks of treatment due to persistent insomnia. Thus, fluvoxamine may prove useful in the treatment of bulimic patients with its favorable toxicity profile and its notable lack of cardiovascular toxicity (Prager, Cimander, Wagner, Schnitker, & Koch, 1986; Ross, 1983). This is of particular importance to bulimic patients who frequently develop electrolyte abnormalities as a result of excessive vomiting, leading to a detrimental effect on cardiac function.

Another interesting point, especially in these patients, was the significant decrease in their body weight which was not reported in other trials with serotonergic compounds (Solymon, Solymon, & Ledwidge, 1989; Freeman & Hampson, 1987).

To date, publications relating to the use of selective 5-HT reuptake inhibitors in the treatment of bulimia only include fluoxetine. In an open trial, 10 bulimics were treated with 60 to 80 mg of fluoxetine daily (Freeman & Hampson, 1987). Seven of these patients stopped their bulimic behavior completely, 2 improved, and 1 was unchanged. In two large placebo-controlled trials with bulimic women, fluoxetine (60 mg/day) was significantly superior to placebo in decreasing the frequency of binge eating and vomiting episodes (Enas, Pope, & Velvine, 1989; Fluoxetine Bulimia Nervosa Collaborative Study Group, 1992).

Other drugs known to potentiate 5-HT function have also been shown to improve symptoms of bulimia nervosa. Thus, the acute administration of fenfluoramine—a drug that decreases 5-HT release—inhibited binge eating and vomiting in bulimia nervosa patients (Robinson, Checkley, & Russel, 1985). Trazodone, an antidepressant with

mainly serotonergic effects, produced a positive effect in 10 bulimic patients in an open study (Solymon et al., 1989).

The results of this uncontrolled open trial should be interpreted with care, although they are comparable to the results obtained in similar trials with trazodone (Solymon et al., 1989) and fluoxetine (Freeman & Hampson, 1987). The results of the present trial suggest that fluvoxamine is a safe and effective treatment for bulimia nervosa; however, further double-blind trials are necessary to support the findings. In addition, we must conduct studies with longer observation periods in order to find out if the improvement in bulimic symptoms persists beyond the testing period.

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