Effects of Behavioral Therapy on Weight Loss in Overweight and Obese Patients With Schizophrenia or Schizoaffective Disorder

Jaspreet S. Brar, M.D., M.P.H.; Rohan Ganguli, M.D.; Gahan Pandina, Ph.D.; Ibrahim Turkoz, M.S.; Sally Berry, M.D.; and Ramy Mahmoud, M.D.

Received April 8, 2004; accepted Aug. 8, 2004. From the Western Psychiatric Institute and Clinic, Pittsburgh, Pa. (Drs. Brar and Ganguli); Janssen Medical Affairs, LLC, Titusville, N.J. (Drs. Pandina and Mahmoud and Mr. Turkoz); and Johnson & Johnson Pharmaceutical Research & Development, LLC, Titusville, N.J. (Dr. Berry).

Supported by Janssen Pharmaceutica Products, LP, Titusville, N.J.

Presented in part at the 43rd annual meeting of the New Clinical Drug Evaluation Unit, May 27–30, 2003, Boca Raton, Fla.

Dr. Ganguli has been a consultant for and received honoraria from Janssen, Eli Lilly, Pfizer, and Bristol-Myers Squibb; has received grant/research support from Janssen, Eli Lilly, and Bristol-Myers Squibb; and has participated in speakers/advisory boards of Janssen, Pfizer, and Bristol-Myers Squibb. Drs. Pandina and Mahmoud and Mr. Turkoz are employees of Janssen. Dr. Berry is an employee of Johnson & Johnson.

Corresponding author and reprints: Rohan Ganguli, M.D., Department of Psychiatry, Pathology and Health & Community Systems, UPMC Health System, Western Psychiatric Institute and Clinic, 3811 O'Hara St., Pittsburgh, PA 15213-2593 (e-mail: GanguliR@msx.upmc.edu).

Background: Obesity is common in persons with schizophrenia. Besides its adverse health effects, obesity reduces quality of life and contributes to the social stigma of schizophrenia.

Method: This 14-week, multicenter, open-label, rater-blinded, randomized study evaluated the effects of a group-based behavioral treatment (BT) for weight loss in overweight and obese stable patients with DSM-IV schizophrenia or schizoaffective disorder who had been switched from olanzapine to risperidone. Participants were randomly assigned to receive BT or usual clinical care (UC). BT included 20 sessions during which patients were taught to reduce caloric intake. In UC, patients were encouraged to lose weight but received no special advice about weight reduction. The primary outcome measure was change in body weight.

Results: Seventy-two patients were enrolled. The mean ± SD weight loss at endpoint was significant in both groups ($p < .05$) and numerically greater in patients receiving BT than in those receiving UC (–2.0 ± 3.79 and –1.1 ± 3.11 kg, respectively). More patients in the BT group than in the UC group had lost ≥ 5% of their body weight at endpoint (26.5% [9/34] and 10.8% [4/37], respectively; $p = .082$). A post hoc analysis of patients attending at least 1 BT session showed that significantly more patients in the BT than the UC group had lost ≥ 5% of their body weight at endpoint (32.1% [9/28] vs. 10.8% [4/37], respectively, $p = .038$) and at week 14 (completer population; 40.9% [9/22] and 14.3% [4/28], respectively, $p = .027$).

Conclusion: BT may be an effective method for weight reduction in patients with chronic psychotic illness.

(J Clin Psychiatry 2005;66:205–212)

The prevalence of obesity is higher among patients with schizophrenia than in the general population.[1] Although this phenomenon has in large part been attributed to atypical or conventional antipsychotic medications, a higher than usual prevalence has also been observed in unmedicated patients.[2] Obesity in patients with schizophrenia was reported in the literature before the introduction of neuroleptic medications and was thought to signify a favorable outcome.[3,4] A few recent studies have also shown similar associations between weight gain and clinical response, arguing that the receptors involved in body weight and food intake may also mediate the therapeutic effects of antipsychotic medications.[5,6] However, these beneficial effects, if present, are offset by the physical and psychosocial consequences of obesity.

Obesity is associated with an increased risk of coronary heart disease, diabetes mellitus, hypertension, and other illnesses.[7] Contributing further to the risk of cardiovascular disease are metabolic abnormalities, including glucose and lipid dysregulation, which have been reported with some atypical antipsychotics.[8–11] These abnormalities play a role in the higher mortality observed in patients with schizophrenia.[12] From a psychosocial perspective, patients regard weight gain as one of the most undesirable side effects of medication, and weight gain is an important factor in noncompliance.[13] Obesity also reduces self-esteem, quality of life, well-being, and vitality

and contributes to the disability and social stigma associated with schizophrenia.[14,15]

Weight gain in schizophrenia has a multifactorial etiology involving clinical, physiologic, genetic, psychosocial, and environmental factors. The clinical and physiologic causes of obesity are unclear, but multiple mechanisms have been suggested to explain antipsychotic-induced weight gain, including serotonergic, dopaminergic, adrenergic, histaminergic, glutamatergic, and cholinergic blockade, as well as metabolic effects related to glucose and leptin regulation.[16–19] Therefore, it is not unexpected that individual agents, which have different receptor-binding profiles,[20] each have different propensities to induce weight gain. Clozapine and olanzapine are most likely to induce weight gain, whereas risperidone is less likely and ziprasidone the least.[19,21] As more evidence emerges about the different potential of individual agents for inducing weight gain and associated metabolic abnormalities, reasons for switching stable antipsychotic-treated patients from one agent to another may become more compelling.

Nutrition is an important environmental factor related to obesity, and only a handful of studies have examined diet or dietary choices and their association, if any, with body weight in patients with schizophrenia. Studies completed in the United Kingdom have shown that the diet in patients with schizophrenia is high in fat and low in fiber and vitamins as compared with that of the general population.[22] Other studies have suggested that obesity in schizophrenia may result from poor dietary choices or from a medication-related side effect.[23,24] In a survey of outpatients with schizophrenia in remission, the authors observed that patients with schizophrenia consumed larger quantities of food than a reference population.[24] Although there were no significant differences in the various components of foods consumed (e.g., the percentage of carbohydrates and saturated and unsaturated fats), patients with schizophrenia consumed larger quantities, and hence more calories, than age- and gender-referenced controls.

The efficacy and safety of pharmacologic treatments for obesity in patients with schizophrenia have not yet been established. Adjunctive use of fluoxetine, sibutramine, amantadine, and topiramate has shown variable efficacy for inducing weight loss in these patients, but the use of these agents may be limited by their side effects.[18] There is also concern about adding weight-reducing agents to a regimen of psychotropic agents, especially as the agents with the highest efficacy have the potential to worsen psychotic symptoms. Furthermore, polypharmacy increases the cost of care. Therefore, nonpharmacologic approaches have appeal as complementary approaches to pharmacotherapy in improving health and well-being for schizophrenia patients. Behavioral approaches for the management of various functional domains, such as those aimed at improving medication compliance and social skills, have shown promise in schizophrenia. Therefore, behavioral approaches for weight reduction aimed at reducing caloric intake and increasing energy expenditure are logically appealing.

A review of studies examining behavioral treatments for weight reduction in patients with schizophrenia is presented in Table 1. Fewer than half of the studies had a comparator group, and only 3 studies randomly assigned patients to the behavioral weight-loss intervention.[26,30] Thus, for the majority of studies, a selection bias resulting from enrollment of those patients who were already motivated to lose weight cannot be ruled out. With the exception of the case report,[25] the mean weight loss ranged from 0.06 to 13.1 lb over a period of 10 to 24 weeks. Despite the deficiencies in methodology, the results of these studies suggest that behavioral interventions are effective for producing modest weight loss.

We report the results of an open-label, randomized study designed to evaluate the effects of behavioral treatment on weight loss in overweight and obese patients with schizophrenia or schizoaffective disorder. This 14-week study was the second phase of a 20-week study designed to evaluate the safety and efficacy of 3 paradigms for switching stable patients with schizophrenia or schizoaffective disorder from olanzapine to risperidone (R.G. et al., manuscript submitted). At phase 1 baseline, patients were randomly assigned to 1 of 3 switch paradigms as follows: Abrupt strategy (no overlap of risperidone and olanzapine), Gradual 1 strategy (50% reduction in olanzapine while titrating risperidone), and Gradual 2 strategy (100% of olanzapine dose for 1 week while titrating risperidone, decreasing to 50% for 1 week, then discontinuation). Patients were subsequently treated with risperidone for 6 weeks.

METHOD

At the end of the first 6-week phase, patients with a body mass index (BMI) of > 26 kg/m^2 were invited to participate in a weight-loss treatment program, and consenting subjects were randomly assigned to either 14 weeks of behavioral treatment (BT) for weight loss or usual clinical care (UC). A BMI of > 26 kg/m^2 was chosen as an inclusion criterion for the study for 2 reasons: first, it was felt that patients who barely met the standard criterion for overweight (BMI > 25 kg/m^2) may not have sufficient motivation to lose weight and, second, given small fluctuations in daily body weight, this higher criterion made it less likely that patients whose weight fluctuated between normal and overweight would be included. BT therapy included 20 sessions over a 14-week period, during which patients were taught various behavioral techniques for weight loss. UC involved no additional interventions, but did include monthly measurement of weight. The trial was conducted in accordance with current International Conference on Harmonisation (ICH)–

Table 1. Studies Examining Behavioral Treatment for Weight Reduction in Patients With Schizophrenia

Study	N	Technique	Control Group	Randomized	Dropout Rate	Duration	Weight Change
Moore and Crum, 1969[25]	1	Operant conditioning	No	No	NA (single case study)	26 wk	Loss of 35 lb
Rotatori et al, 1980[26]	14	Behavioral technique to reduce caloric intake	Yes	Yes	No dropouts	14 wk	Mean loss of 7.3 lb
Wirshing et al, 1999[19]	92	Stepwise intervention with food diary, exercise, and group support	No	No	NA (retrospective chart review)	6–15 mo	Reduction in weight gain in patients treated with olanzapine
Aquila and Emanuel, 2000[27]	31	Dietary counseling, decreased portion size, and support groups	No	No	NA (retrospective study)	1.5 y	No change in weight
Ball et al, 2001[28]	21	Commercial Weight Watchers program	No	No	47.6%	10 wk	Mean loss of 5.1 lb, significant only in men (results for completers)
Ganguli et al, 2001[29]	8	Behavioral technique to reduce caloric intake	Yes	Yes	12.5%	14 wk	Mean loss of 4.17 lb in the behavioral treatment group (results for completers)
Littrell et al, 2003[30]	70	Intensive educational program on nutrition and exercise for prevention of weight gain	Yes	Yes	No dropouts	6 mo	Intervention group lost 0.06 lb, control group gained over 9 lb
Centorrino et al, 2002[31]	17	Diet, lifestyle counseling, and exercise	No	No	Not reported	24 wk	Mean loss of 13.1 lb, lowering of systolic and diastolic BP
Menza et al, 2003[32]	31	Intensive weight control program addressing nutrition, exercise, and behavior	Yes	No	32.3%	12 wk, with 6-mo maintenance	Mean loss of 6.6 lb in intervention group, weight gain in controls (results for completers)
Vreeland et al, 2003[33]	31	Weight control program incorporating nutrition, exercise, and behavioral interventions	Yes	No	13%	12 wk	Mean loss of 2.7 kg in intervention group, 2.9-kg gain in controls (not reported whether results for completers or ITT)
O'Keefe et al, 2003[34]	35	Retrospective chart review of dietitian visit, self-directed diet, weight loss as treatment goal	No	No	NA	Approximately 5 y	Patients who used interventions stopped gaining or lost weight

Abbreviations: BP = blood pressure, ITT = intent-to-treat, NA = not applicable.

Good Clinical Practice guidelines and the Declaration of Helsinki and its subsequent revisions. Written informed consent was obtained from each patient or a relative, guardian, or legal representative.

Patients

Patients were recruited at 19 sites in the United States. Those eligible for inclusion in phase 1 were men and women aged 18 to 65 years with a DSM-IV diagnosis of schizophrenia or schizoaffective disorder who were either outpatients or stable long-term inpatients. All patients were to have been treated with a stable dose of olanzapine for at least 30 days before randomization and to have had no acute exacerbation of psychotic symptoms within the preceding 3 months. Patients were also required to meet at least 1 of the following additional criteria: Positive and Negative Syndrome Scale (PANSS)[35] total score of 60 to 120, BMI > 26 kg/m^2 plus motivation to lose weight, or type 2 diabetes or laboratory abnormalities related to glucose metabolism, including fasting plasma glucose > 80 mg/dL or oral glucose tolerance test 2-hour value > 139 mg/dL. Patients were subsequently eligible to participate in phase 2, the weight management phase of the study, if, in the clinical judgment of the investigator, their psychiatric status was not significantly worse than that determined at phase 1 baseline, their BMI was > 26 kg/m^2, and they were motivated to lose weight.

Patients were excluded if their medical history indicated a previous treatment failure, significant adverse event, or sensitivity related to risperidone; treatment-refractory schizophrenia or schizoaffective disorder; antipsychotic treatment other than olanzapine in the 30 days preceding randomization; or mental retardation, substance dependence, or a serious or unstable concomitant illness.

Behavioral Weight-Loss Treatment

Behavioral treatment for weight reduction is a manual-driven, didactic program that can be taught by most individuals who have had some experience working with the mentally ill in group settings.[36] It is structured in an incremental, stepwise manner that leads toward proficiency as the program matures. Food models are used to perform simulated training sessions. Instructions with simulated exercises provide participants with the opportunity to familiarize themselves with the new techniques taught before going home, practice the techniques in a simulated manner, and receive feedback from the group leader.

Patients randomly assigned to receive BT were to attend 2 therapy sessions per week for 6 weeks

followed by 1 session per week for 8 weeks (a total of 20 sessions). The first session was to occur no later than 2 weeks after week 6 of the phase 1 study. At these sessions, patients were taught the following weight-loss techniques: during weeks 1 and 2, self-monitoring of daily weight and recording of food consumed; weeks 3 and 4, modifying urges to overeat by using a cognitive technique to reinforce abstinence from or postponement of snacks; weeks 5 and 6, decreasing food cues to overeat by limiting eating to 1 physical area and limiting meals to 1 helping only; weeks 7 and 8, developing good eating habits by slowing the pace of eating; weeks 9 and 10, imposing self-control of overeating by leaving some food on the plate; weeks 11 and 12, burning calories by exercising more; and weeks 13 and 14, changing snacking habits and snacks.

The group leader presented the rationale and a detailed description of each of the techniques a week before their implementation. In addition, the technique was also demonstrated in a simulation using food models if necessary. Patients were asked to rehearse the technique with the group leader, who provided feedback on their performance. These instruction and rehearsal sessions were repeated at each visit. At the final session, patients in the BT group were given a written summary of all the techniques taught during the study, as well as basic information about nutrition, and were encouraged to refer to these guidelines frequently and to continue with their efforts to lose weight.

Patients randomly assigned to receive UC were encouraged to lose weight on their own, with no instructions from the investigators. These patients were seen at monthly intervals for anthropometric assessments.

Assessments

The primary outcome measure was the change in body weight. Other efficacy variables were the patients' attendance at BT sessions and scores on the Client Satisfaction Questionnaire (CSQ-8).[37] The CSQ-8 is an 8-item self-rated questionnaire that patients use to assess their satisfaction with the service provided.

Weight was measured at baseline and weeks 4, 8, and 14. Other anthropometric measurements, including height, BMI, slenderness index (height in meters divided by the sum of the wrist width and knee width in meters), waist circumference, and waist-to-hip ratio, were obtained or calculated at baseline and endpoint.

Efficacy assessments included the PANSS, Clinical Global Impressions-Change (CGI-C), and CGI-Severity of Illness (CGI-S).[38] These assessments and the CSQ-8 were completed at baseline and weeks 4, 8, and 14. Adverse events and vital signs were recorded at baseline and regular intervals, and laboratory tests, including hematology and biochemistry, were performed at baseline and endpoint.

Statistical Analysis

Assuming that a common standard deviation is approximately 9 using a 2-group t test with a 2-sided alpha of .05, a sample size of 25 patients in each group would provide 80% power to detect a difference in means of 7 lb of body weight. Assuming a 15% dropout rate after randomization, it was necessary to randomly assign 30 patients to each treatment group (total of 60 patients).

For efficacy measures, including CSQ-8, an intent-to-treat (ITT) analysis was performed such that all patients who received at least 1 dose of study medication and had at least 1 postbaseline measurement were included. The cohort in whom PANSS and CGI scores were analyzed consisted of patients with PANSS total scores of 60 to 120 at baseline.

Change in weight from baseline, both as a categorical variable (if follow-up weight at endpoint was at least 5% less than the weight at baseline, weight loss was present; if not, weight loss was absent) and a continuous variable, was compared in the BT and UC treatment groups. Within-treatment changes were evaluated using a paired t test. All statistical tests were interpreted at the 5% significance level (2-tailed).

Changes in body weight and other anthropometric measures obtained at monthly visits were compared in the 2 treatment groups using a repeated-measures analysis of variance. Between-group differences in number and percentage of subjects with $\geq 5\%$ reduction in weight were analyzed using a logistic regression with treatment and site in the model. Correlations between changes in weight, measures of psychopathology, adverse effect measures, CSQ-8 laboratory assessments, and vital signs were also examined. For the clinical laboratory data, descriptive statistics and pretreatment and posttreatment cross-tabulations (in which the results were classified according to whether they were below, within, or above the normal range) were generated for all tests performed. For PANSS, within-group changes were evaluated using a paired t test, and between-group changes were evaluated using an analysis of covariance with treatment site as a factor and baseline score as a covariate. The CGI scores were compared between groups using the Cochran-Mantel-Haenszel test.

Analyses were performed per study protocol on all patients randomized who received at least 1 dose of study medication, regardless of attendance at any BT sessions. However, several patients attended no BT sessions. Therefore, post hoc analysis was performed on weight measures using an attendee analysis, which included all patients who received at least 1 dose of study medication and attended at least 1 BT session. The post hoc analysis also assessed a completer population, which included attendee patients with week 14 weight data. In addition, since a high proportion of patients were morbidly obese, resulting in a higher mean baseline weight than expected, substan-

Table 2. Baseline Patient Demographics and Clinical Characteristics (ITT analysis)

Variable	Behavioral Treatment (N = 34)	Usual Clinical Care (N = 37)
Sex, N (%)		
Female	18 (52.9)	24 (64.9)
Male	16 (47.1)	13 (35.1)
Race/ethnicity, N (%)		
White	18 (52.9)	17 (45.9)
Hispanic	1 (2.9)	5 (13.5)
Black	13 (38.2)	12 (32.4)
Asian	2 (5.9)	2 (5.4)
Other	0 (0.0)	1 (2.7)
Age, y		
Mean ± SD	40.0 ± 10.1	40.5 ± 10.6
Range	21–59	21–64
Diagnosis, N (%)		
Schizophrenia	21 (61.8)	17 (45.9)
Schizoaffective disorder	13 (38.2)	20 (54.1)
Dose of risperidone, mean (SD), mg/d	4.74 (1.7)	4.19 (1.8)
Concomitant therapy, %		
Sedative-hypnotics	8.8	5.4
Antidepressants	20.6	13.5

Abbreviation: ITT = intent-to-treat.

Table 3. Weight Change at Endpoint (ITT analysis)

Variable	Behavioral Treatment (N = 34)	Usual Clinical Care (N = 37)	p[a]
Weight, mean (SD), kg			
Baseline	101.3 (18.91)	98.9 (28.05)	
Change at endpoint	–2.0 (3.79)	–1.1 (3.11)	.287
Patients with ≥ 5% weight loss at endpoint, N (%)	9 (26.5)	4 (10.8)	.082

[a]Between-group comparisons: analysis of covariance with factors for treatment and site for mean weight change; logistic regression with factors for treatment and site for distribution of categorical weight changes. Values for within-group comparisons of change from baseline were p = .005 for the behavioral treatment group and p = .042 for the usual clinical care group.
Abbreviation: ITT = intent-to-treat.

tial absolute weight loss was less likely to constitute 5% of baseline body weight. Therefore, a post hoc analysis of categorical weight losses of ≥ 3% and ≥ 4% from baseline was performed using a logistic regression with treatment, site, and concomitant medications in the model. Within-group comparisons (baseline to endpoint changes) were made using paired t tests. Between-group comparisons were assessed with analysis of covariance (treatment and site as factors) for mean weight change and with logistic regression (treatment and site as factors) for the distribution of categorical variables.

RESULTS

Of the 123 patients who participated in the 6-week phase 1 of this study, 72 qualified for and were offered behavioral treatment for 14 weeks in phase 2. Following the switch from olanzapine to risperidone in the first phase of this study, no weight loss was observed; however, switching patients to risperidone may have avoided further olanzapine-induced weight gain. The 72 patients were randomly assigned to receive BT (N = 35) or UC (N = 37). One patient in the BT group withdrew consent, did not receive study medication, and was removed from all analyses. Seventy-one patients were included in the ITT analysis (BT, N = 34; UC, N = 37). For the attendee analysis, 6 patients in the BT group dropped out before attending a BT session, leaving 65 patients for this attendee analysis (BT, N = 28; UC, N = 37). Fifty of these patients were completers (BT, N = 22; UC, N = 28). There were no significant differences in reasons for discontinuation between the 2 groups. In both groups, the most common reasons for discontinuation were adverse events (N = 1, both groups), insufficient response (BT, N = 1; UC, N = 0), and lost to follow-up (BT, N = 2; UC, N = 1).

There were no between-group differences in patient demographics or baseline clinical characteristics (Table 2). The BT group had a slightly smaller proportion of women (52.9% [18/34] and 64.9% [24/37], respectively), but this difference was not statistically significant. The mean dose of risperidone was 4.74 mg/day in the BT group and 4.19 mg/day in the UC group. Twenty-eight patients in the BT group attended at least 1 BT session, 21 attended at least 14 sessions, and 15 attended all 20 sessions.

Weight Loss and Anthropometric Measurements

Statistically significant weight loss was reported at endpoint in both treatment groups (mean ± SD: BT, –2.0 ± 3.79 kg, p = .005; UC, –1.1 ± 3.11 kg, p = .042); the between-group difference did not reach statistical significance in this sample (Table 3). At endpoint, 9 patients (26.5%) in the BT group and 4 patients (10.8%) in the UC group lost ≥ 5% of their baseline body weight (p = .082; Table 3).

In the attendee population (patients who attended at least 1 BT session), mean weight-loss results were similar to those in the ITT group (Table 4). However, significantly more attendees in the BT group than the UC group lost ≥ 5% of their baseline body weight at endpoint (32.1% [9/28] and 10.8% [4/37], respectively, p = .038; Table 4, Figure 1), as well as in the completer population (40.9% [9/22] and 14.3% [4/28], respectively, p = .027; Table 4, Figure 1). Results were similar for percentages of patients with weight loss of ≥ 3% and ≥ 4% (Table 4).

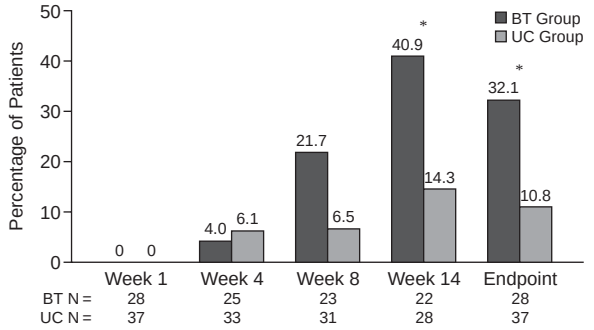
In the ITT population, the BMI also decreased significantly from baseline to endpoint in both the BT group (–0.9 ± 1.38; p = .003) and the UC group (–0.5 ± 1.19; p = .029). There was no significant between- or within-group difference at endpoint in the slenderness index or waist-to-hip ratio, although patients who lost weight did experience reductions in both waist and hip circumference.

Table 4. Weight Change at Endpoint (post hoc analysis)

Weight Variable	Attendees: Behavioral Treatment (N = 28)	Attendees: Usual Clinical Care (N = 37)	Attendees: p[a]	Completers: Behavioral Treatment (N = 22)	Completers: Usual Clinical Care (N = 28)	Completers: p[a]
Baseline weight, mean (SD), kg	103.5 (19.3)	98.9 (28.1)		96.0 (16.2)	97.5 (30.8)	
Change from baseline, mean (SD), kg	–2.3 (4.0)	–1.1 (3.1)	.120	–3.2 (3.8)	–1.4 (3.2)	.076
Within-group p value for change from baseline	.005	.042		.001	.027	
Weight loss from baseline to endpoint, N (%)						
≥ 3%	14 (50.0)	10 (27.0)	.069	14 (63.6)	8 (28.6)	.021
≥ 4%	12 (42.9)	6 (16.2)	.025	12 (54.5)	6 (21.4)	.021
≥ 5%	9 (32.1)	4 (10.8)	.038	9 (40.9)	4 (14.3)	.027

[a]Between-group comparisons: analysis of covariance with factors for treatment and site for mean weight change; logistic regression with factors for treatment and site for distribution of categorical weight changes.

Figure 1. Percentage of Patients With ≥ 5% Weight Reduction From Baseline in the Behavioral Treatment (BT) and Usual Clinical Care (UC) Groups (attendee population)



*p < .05 between groups.

Schizophrenia-Related Assessments and Client Satisfaction

Significant (p < .001) reductions in mean PANSS total, positive, and anxiety/depression scores were reported in the total patient population during phase 1 of this study and were maintained during the 14-week weight-loss phase. Mean ± SD total PANSS scores in the BT group were 63.7 ± 17.43 and 63.9 ± 22.61 at baseline and endpoint, respectively (p = .927), and in the UC group were 61.7 ± 16.81 and 60.9 ± 16.27 at baseline and endpoint, respectively (p = .728). There was no significant difference between the 2 groups in mean PANSS total scores at baseline (p = .650) or at endpoint (p = .672).

The distributions of CGI-S ratings at baseline and weeks 1, 4, 8, 14, and endpoint were not significantly different in the BT and UC groups. However, the proportion of patients who had a CGI-C rating of "much improved" or "very much improved" was greater for the BT than the UC group at endpoint (39.4% and 27.0%, respectively; p = .49). In the attendee analysis, this difference was even more apparent (46.4% [13/28] and 27.0% [10/37], BT and UC, respectively; p = .41).

The mean CSQ-8 score in the BT group increased significantly from baseline to endpoint (28.9 ± 2.77 to 30.1 ± 2.42, respectively; p = .015), whereas that in the UC group remained unchanged. The mean change in CSQ-8 score from baseline to endpoint was also significantly greater in the BT group than in the UC group (p = .004). Endpoint scores were 30.1 ± 2.42 and 27.8 ± 3.52 in the BT and UC groups, respectively.

Cardiovascular-Related Outcomes

In the ITT population, the BT group demonstrated statistically significant decreases in mean systolic blood pressure. The mean sitting systolic blood pressure in that group decreased from 122.7 ± 14.58 mm Hg at baseline to 117.8 ± 12.25 mm Hg at week 14 (p = .019). Mean standing systolic pressure was also decreased from baseline at week 14 (124.0 ± 15.35 mm Hg and 117.8 ± 11.73 mm Hg at baseline and week 14, respectively; p = .006) as well as at endpoint (118.4 ± 13.0 mm Hg; p = .014). No significant changes in systolic blood pressure were reported in the UC group. The mean sitting systolic blood pressure was 122.3 ± 15.33 mm Hg at baseline and 120.6 ± 11.92 mm Hg at week 14 (p = .514). The mean standing systolic blood pressure was 121.8 ± 13.46 mm Hg at baseline and 121.5 ± 10.28 mm Hg at week 14 (p = .710). The mean diastolic blood pressure, heart rate, and vital signs did not change significantly from baseline to endpoint in either treatment group.

DISCUSSION

This study demonstrates the feasibility and effectiveness of a specific behavioral program for weight reduction in patients with schizophrenia and schizoaffective disorder. Approximately 70% of the total sample completed the study. The attendance rates at BT sessions indi-

cate that the majority of outpatients with schizophrenia will voluntarily attend such a program, if motivated to do so. These attendance rates are similar to those reported in a study of the Weight Watchers weight loss program (once-weekly meetings presenting information on a dietary plan coupled with positive reinforcement for weight loss) that involved outpatients with schizophrenia receiving olanzapine.[28] In that study, 66% of patients attended at least 1 meeting, and 52% completed the program.[28]

Among patients in the present study who completed the behavioral weight loss program, half of the sample was able to lose at least 4% of their baseline weight within a period of 14 weeks. Differences between groups using the 5% cutoff were statistically significant in this sample, even though the study was not adequately powered to detect this (a sample of 190 patients should have been needed to detect this difference). While this relatively modest weight loss could be viewed as cosmetically insignificant, it has been shown that modest weight loss in moderate or severely obese individuals may be associated with health benefits.[39] Among obese patients with diabetes, a 5% reduction in body weight has been associated with an improvement in glycemic control,[40] less than 5% reduction with a decrease in serum triglycerides and insulin,[41] and weight loss as little as 1 kg with a 3- to 4-month prolonged survival.[42] Among obese patients with hypertension, modest weight loss has been associated with demonstrable benefits in blood pressure.[43] Eliahou and colleagues[44] have shown that for every 1% of weight lost (in percent overweight), a mean change of 1.9 mm Hg (systolic) and 1.3 mm Hg (diastolic) can be expected. A reduction of waist circumference during weight loss is also associated with cardiovascular benefits.[45] This cumulative evidence suggests that a continuum of health benefits is associated with a continuum of weight loss.

Also of interest in this study is the positive effect of BT on overall client satisfaction as well as global severity of illness. These effects may reflect the benefits of positive psychosocial interactions associated with BT session attendance, as well as improved body image. Among patients who attended at least 1 BT session, the percentage of patients who were "much" or "very much" improved on the CGI-C was approximately twice that of the UC group (46% vs. 27%), although the difference was not significant.

Successful behavioral strategies for weight management should contain the following key elements: behavioral modification through self-monitoring and stimulus control, diet, and exercise.[46] Differences emerge in the complexity of the instructions, the training required to implement the various programs, and the costs of the dietary recommendations. The behavioral program used in this study has appeal because, in contrast to other programs, it does not require special training to implement, has a very simple content, emphasizes reduction in the quantity of food taken in rather than extensive changes in food choice, and does not require purchase of special food supplements. Furthermore, the general applicability of this manual-based program was demonstrated by the ease with which group leaders across 19 sites were able to implement it. Thus, this behavioral treatment could emerge as a desirable nonpharmacologic option for use in any community setting that treats the chronically mentally ill.

Weight management for patients with schizophrenia is seldom emphasized and remains a poorly researched area, despite the high rates of obesity and associated medical comorbidity documented in this population. In fact, patients with chronic mental illnesses are frequently excluded from controlled weight-management studies, further compromising the health and well-being of an already disenfranchised population. In a survey completed by the RAND Corporation, it was observed that obesity has an impact on chronic medical conditions and health-related quality of life that is similar to the effects of poverty, smoking, and problem drinking on these outcomes.[47] These physical and psychological impairments are compounded in a population that also has a high prevalence of smoking[48] and low socioeconomic status.[49]

The benefits of atypical antipsychotics in the treatment of patients with psychotic illnesses outweigh the risk for weight gain; however, appropriate initial choice of an antipsychotic with a lower liability for weight gain or switching patients from one with a high liability for weight gain to one with a lower liability should also be considered as part of a weight-control strategy. Maintenance of weight following a switch from olanzapine to risperidone (as well as statistically significant weight gain following a switch from risperidone to olanzapine) was observed in the present study and has also been reported elsewhere.[50] In addition, since both the BT and UC groups lost weight in the present study, the switch to risperidone may have contributed to weight loss over the longer term.

Although this was a controlled, randomized, multicenter study, limitations include its open-label design and the lack of information about the persistence of weight loss. Furthermore, the exact mechanisms by which the positive effects on weight loss occurred might have been better elucidated by recording patient lifestyle changes and incorporating additional control groups, such as a group in which social interactions similar to those in the BT group occurred without imparting weight loss techniques or a group of overweight patients who were not encouraged to make efforts to lose weight.

This study provided evidence that behavioral therapy can reduce weight gain in obese patients with schizophrenia receiving atypical antipsychotics. However, the weight reduction observed was modest, and thus the importance of choosing an antipsychotic agent with a low propensity for weight gain remains undiminished. Further research is needed to fully elucidate the role of behavioral therapy in reducing weight gain.

Drug names: amantadine (Symmetrel and others), clozapine (Clozaril, Fazaclo, and others), fluoxetine (Prozac and others), olanzapine (Zyprexa), risperidone (Risperdal), sibutramine (Meridia), topiramate (Topamax), ziprasidone (Geodon).

REFERENCES

1. Homel P, Casey D, Allison DB. Changes in body mass index for individuals with and without schizophrenia, 1987–1996. Schizophr Res 2002;55:277–284
2. Theisen FM, Linden A, Geller F, et al. Prevalence of obesity in adolescent and young adult patients with and without schizophrenia and in relationship to antipsychotic medication. J Psychiatr Res 2001;35:339–345
3. Kraepelin E. Dementia Praecox and Paraphrenia. Barkley RM, trans. Edinburgh, Scotland: E & S Livingstone; 1919
4. Jaspers K. General Psychopathology. Hoenig J, Hamilton MW, trans. Chicago, Ill: University of Chicago Press; 1963
5. Basson BR, Kinon BJ, Taylor CC, et al. Factors influencing acute weight change in patients with schizophrenia treated with olanzapine, haloperidol, or risperidone. J Clin Psychiatry 2001;62:231–238
6. Czobor P, Volavka J, Sheitman B, et al. Antipsychotic-induced weight gain and therapeutic response: a differential association. J Clin Psychopharmacol 2002;22:244–251
7. Pi-Sunyer FX. The obesity epidemic: pathophysiology and consequences of obesity. Obes Res 2002;10(suppl 2):97S–104S
8. Goldman LS. Medical illness in patients with schizophrenia. J Clin Psychiatry 1999;60(suppl 21):10–15
9. Lindenmayer J-P, Nathan A-M, Smith RC. Hyperglycemia associated with the use of atypical antipsychotics. J Clin Psychiatry 2001;62 (suppl 23):30–38
10. Meyer JM. Novel antipsychotics and severe hyperlipidemia. J Clin Psychopharmacol 2001;21:369–374
11. Wirshing DA, Spellberg BJ, Erhart SM, et al. Novel antipsychotics and new onset diabetes. Biol Psychiatry 1998;44:778–783
12. Simpson JC, Tsuang MT. Mortality among patients with schizophrenia. Schizophr Bull 1996;22:485–499
13. Weiden P, Mackell J. Differing side effect burdens with newer antipsychotics [poster]. Presented at the 39th annual meeting of the New Clinical Drug Evaluation Unit; June 1–4, 1999; Boca Raton, Fla
14. Allison DB, Mackell JA, McDonnell DD. The impact of weight gain on quality of life among persons with schizophrenia. Psychiatr Serv 2003;54:565–567
15. Strassnig M, Brar JS, Ganguli R. Body mass index and quality of life in community-dwelling patients with schizophrenia. Schizophr Res 2003;62:73–76
16. Green AI, Patel JK, Goisman RM, et al. Weight gain from novel antipsychotic drugs: need for action. Gen Hosp Psychiatry 2000;22:224–235
17. Stanton JM. Weight gain associated with neuroleptic medication: a review. Schizophr Bull 1995;21:463–472
18. Werneke U, Taylor D, Sanders TA. Options for pharmacological management of obesity in patients treated with atypical antipsychotics. Int Clin Psychopharmacol 2002;17:145–160
19. Wirshing DA, Wirshing WC, Kysar L, et al. Novel antipsychotics: comparison of weight gain liabilities. J Clin Psychiatry 1999;60:358–363
20. Bymaster FP, Calligaro DO, Falcone JF, et al. Radioreceptor binding profile of the atypical antipsychotic olanzapine. Neuropsychopharmacology 1996;14:87–96
21. Allison DB, Mentore JL, Heo M, et al. Antipsychotic-induced weight gain: a comprehensive research synthesis. Am J Psychiatry 1999;156: 1686–1696
22. McCreadie R, Macdonald E, Blacklock C, et al. Dietary intake of schizophrenic patients in Nithsdale, Scotland: case-control study. BMJ 1998;317:784–785
23. Brown S, Birtwistle J, Roe L, et al. The unhealthy lifestyle of people with schizophrenia. Psychol Med 1999;29:697–701
24. Strassnig M, Brar JS, Ganguli R. Nutritional assessment of patients with schizophrenia: a preliminary study. Schizophr Bull 2003;29:393–397
25. Moore CH, Crum BC. Weight reduction in a chronic schizophrenic by means of operant conditioning procedures: a case study. Behav Res Ther 1969;7:129–131
26. Rotatori AF, Fox R, Wicks A. Weight loss with psychiatric residents in a behavioral self control program. Psychol Rep 1980;46:483–486
27. Aquila R, Emanuel M. Interventions for weight gain in adults treated with novel antipsychotics. Prim Care Companion J Clin Psychiatry 2000;2:20–23
28. Ball MP, Coons VB, Buchanan RW. A program for treating olanzapine-related weight gain. Psychiatr Serv 2001;52:967–969
29. Ganguli R, Brar JS, Mullen B. Behavioral treatment for weight loss in patients with schizophrenia [poster]. Presented at the 53rd Institute of Psychiatric Services; October 10–14, 2001; Orlando, Fla
30. Littrell KH, Hilligoss NM, Kirshner CD, et al. The effects of an educational intervention on antipsychotic-induced weight gain. J Nurs Scholarsh 2003;35:237–241
31. Centorrino F, Wurtman JJ, Duca KK, et al. Comprehensive weight loss program for overweight subjects treated with atypical antipsychotics [poster]. Presented at the 155th annual meeting of the American Psychiatric Association; May 18–23, 2002; Philadelphia, Pa
32. Menza M, Vreeland B, Minsky S, et al. Managing weight gain in patients with schizophrenia: twelve months of data on the Healthy Living Program [poster]. Presented at the 156th annual meeting of the American Psychiatric Association; May 17–22, 2003; San Francisco, Calif
33. Vreeland B, Minsky S, Menza M, et al. A program for managing weight gain associated with atypical antipsychotics. Psychiatr Serv 2003;54: 1155–1157
34. O'Keefe CD, Noordsy DL, Liss TB, et al. Reversal of antipsychotic-associated weight gain. J Clin Psychiatry 2003;64:907–912
35. Kay SR, Opler LA, Fiszbein A. The Positive and Negative Syndrome Scale (PANSS Manual). North Tonawanda, NY: Multi-Health System; 1986
36. Rotatori AF, Fox R, Switzky H. A parent-teacher administered weight reduction program for obese Down's syndrome adolescents. J Behav Ther Exp Psychiatry 1979;10:339–341
37. Attkisson CC, Zwick R. The Client Satisfaction Questionnaire: psychometric properties and correlations with service utilization and psychotherapy outcome. Eval Program Plann 1982;5:233–237
38. Guy W. ECDEU Assessment Manual for Psychopathology. US Dept Health, Education, and Welfare publication (ADM) 76-338. Rockville, Md: National Institute of Mental Health; 1976
39. Pi-Sunyer FX. Short-term medical benefits and adverse effects of weight loss. Ann Intern Med 1993;119(7 pt 2):722–726
40. Stanik S, Marcus R. Insulin secretion improves following dietary control of plasma glucose in severely hyperglycemic obese patients. Metabolism 1980:29:346–350
41. Wing RR, Koeske R, Epstein LH, et al. Long-term effects of modest weight loss in type II diabetic patients. Arch Intern Med 1987;147: 1749–1753
42. Lean MEJ, Powrie JK, Anderson AS, et al. Obesity, weight loss and prognosis in type 2 diabetes. Diabet Med 1990;7:228–233
43. Sonne-Holm S, Sorensen TI, Jensen G, et al. Independent effects of weight change and attained body weight on prevalence of arterial hypertension in obese and non-obese men. BMJ 1989;299:767–770
44. Eliahou HE, Iaina A, Gaon T, et al. Body weight reduction necessary to attain normotension in the overweight hypertensive patient. Int J Obes 1981;5(suppl 1):157–163
45. Han TS, van Leer EM, Seidell JC, et al. Waist circumference action levels in the identification of cardiovascular risk factors: prevalence study in a random sample. BMJ 1995;311:1401–1405
46. Serdula MK, Mokdad AH, Williamson DF, et al. Prevalence of attempting weight loss and strategies for controlling weight. JAMA 1999;282:1353–1358
47. Sturm R, Wells KB. Does obesity contribute as much to morbidity as poverty or smoking? Public Health 2001;115:229–235
48. Hughes JR, Hatsukami DK, Mitchell JE, et al. Prevalence of smoking among psychiatric outpatients. Am J Psychiatry 1986;143:993–997
49. Dohrenwend, BP. Socioeconomic status (SES) and psychiatric disorders: are the issues still compelling? Soc Psychiatry Psychiatr Epidemiol 1990; 25:41–47
50. Reid LD, Renner BT, Bengtson MA, et al. Weight change after an atypical antipsychotic switch. Ann Pharmacother 2003;37:1381–1386