Weight Management Program for Treatment-Emergent Weight Gain in Olanzapine-Treated Patients With Schizophrenia or Schizoaffective Disorder: A 12-Week Randomized Controlled Clinical Trial

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Background: The main objective was to assess the efficacy of a weight management program designed for outpatients taking olanzapine for schizophrenia or schizoaffective disorder and to compare these patients with a randomized control group. The effects of the weight management program were also assessed with regard to safety and quality of life.

Method: Forty-eight patients were enrolled in a 12-week, randomized, multicenter weight management study. Thirty-three patients were randomly allocated to an intervention group in which they received olanzapine within a weight management program. Fifteen patients were allocated to a control group in which they were given olanzapine treatment as usual outpatients. Weight, body mass index (BMI), and measurements of safety and quality of life were evaluated. The study was conducted from January 7, 2003, to September 16, 2003.

Results: Thirty-six patients (75%) completed this study. We found significant differences in weight (–3.94 ± 3.63 kg vs. –1.48 ± 1.88 kg, p = .006) and BMI (–1.50 ± 1.34 vs. –0.59 ± 0.73, p = .007) change from baseline to endpoint between the intervention and control groups, respectively. Significant differences in weight reduction were initially observed at week 8 (p = .040). No significant differences were found with regard to the safety outcomes. When the ratio of low-density lipoproteins to high-density lipoproteins was calculated, change from baseline was greater in the intervention group than the control group (–0.19 vs. –0.04), but the difference was not statistically significant (p = .556). After the completion of the weight management program, there was a trend toward statistical difference in the physical health score changes between the weight management and control groups (1.12 in the intervention group vs. –0.93 in the control group, p = .067).

Conclusion: The weight management program was effective in terms of weight reduction in patients with schizophrenia or schizoaffective disorder taking olanzapine and was also found to be safe in terms of psychiatric symptoms, vital signs, and laboratory data. In addition, such a weight management program might improve quality of life in patients with schizophrenia or schizoaffective disorder with respect to their physical well-being.

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Obesity is a serious medical condition and a well-documented threat to health and longevity due primarily to the association of obesity with hypertension, type 2 diabetes mellitus, coronary heart disease, stroke, gallbladder disease, osteoarthritis, sleep apnea, respiratory problems, and some varieties of cancer.[1,2] In patients with schizophrenia, treatment with many antipsychotic agents is associated with weight gain, and weight gain is a common cause of noncompliance with antipsychotic treatment, often resulting in relapses of the illness.[3]

The atypical antipsychotics have been found to reduce the risk of extrapyramidal symptoms (EPS) and tardive dyskinesia (TD); however, concerns regarding weight gain have increased in the treatment of schizophrenia. Although all atypical antipsychotics are associated with some degree of weight gain, the 2 agents associated with the highest weight gain are clozapine and olanzapine.[4–6] According to the report of Allison et al.,[4] these agents are estimated to produce between 4 and 4.5 kg of weight gain at 10 weeks of treatment with a standard dose. In a cross-sectional study investigating the treatment-emergent adverse effects of antipsychotics in the clinical setting, Bobes et al.[7] reported that patients receiving olanzapine exhibited significantly greater weight gain than those

treated with risperidone or haloperidol. Ziprasidone, however, proved to induce no weight gain, or only minimal weight gain, in patients who were studied for up to 1 year.[8]

The treatment of antipsychotic-associated weight gain has included 1 of 2 approaches: behavioral management and pharmacologic management. Few current data are available with regard to pharmacologic management. Some case studies have reported the exacerbation of psychotic symptoms caused by the use of antiobesity agents.[9,10] Although likelihood of psychosis exacerbation was lowered by the use of peripherally acting agents indicated for weight loss, careful clinical trials of antiobesity agents are warranted in patients with schizophrenia. However, Faulkner et al.[11] suggested that the widespread use of pharmacologic intervention might be inadvisable and that both dietary and exercise counseling, as a behavioral modification program, would be necessary for sustained weight control in cases of schizophrenia. According to the guidelines of the U.S. National Heart, Lung, and Blood Institute,[12] treatment strategies for overweight and obesity include modifications in diet, behavior, and physical activity. Combined treatment, incorporating all 3 approaches, has proven to be the most successful scheme.

Thus far, no weight management programs specifically established for patients with schizophrenia have been reported. Furthermore, most studies on the efficacy of strategies for the reduction of weight gain during treatment with antipsychotics have been limited to descriptive clinical trials, with the consistent shortcomings of small subject numbers and the absence of a control group. The main aim of this study was to evaluate the efficacy of a weight management program designed for outpatients taking olanzapine for the treatment of schizophrenia or schizoaffective disorder and to compare those patients with a randomized control group. We also assessed the effects of this weight management program on safety and quality of life (QOL).

METHOD

Subjects

Forty-eight outpatients with schizophrenia or schizoaffective disorder, diagnosed using DSM-IV criteria, participated in a 12-week, randomized, multicenter weight management study. This study was carried out at 4 clinical centers from January 7, 2003, to September 16, 2003. Written informed consent was obtained from all subjects prior to enrollment, and institutional review board approval was obtained for this study.

Included in this study were men and women between 19 and 64 years of age. These patients had no history of acute manic, hypomanic, or psychotic states within 4 weeks prior to the beginning of this study. All study subjects had been taking olanzapine (5–20 mg/day) for at least 12 weeks before the study began and had experienced weight gains of more than 7% of body weight while receiving olanzapine prior to entering the study.

Exclusion criteria were as follows: pregnant or breastfeeding, Positive and Negative Syndrome Scale (PANSS) score > 70, severe medical disease, hyperthyroidism or hypothyroidism, any history of seizure disorder, diagnosis of DSM-IV substance dependence within 2 months prior to this study, and alanine transaminase (ALT)/aspartate transaminase (AST) levels greater than 200% of the upper normal limit.

To determine a sample size, a sample size analysis was used, and the number of study subjects to be enrolled was 87. Fifty-five patients were recruited, and, after screening evaluation, 48 patients were enrolled. With regard to the allocation of patients to either the intervention or the control group, a ratio of 2 to 1 was determined. We used the allocation ratio of 2 to 1 from an ethical point of view, as the intervention group was expected to be more beneficial to the patients than the control group. Thirty-three patients were randomly allocated to the intervention group, in which the patients took olanzapine with a weight management program, and 15 patients were allocated to the control group, in which they were given olanzapine treatment as usual outpatients. Of these patients, 36 (22 in the intervention group, 14 in the control group) completed the study.

The demographic and clinical characteristics of the 48 subjects enrolled in this study are shown in Table 1. Patients in the control group had significantly higher systolic blood pressure at baseline. There were no significant differences in other variables between the 2 groups. The difference in the distribution of diagnoses between the 2 groups was not significant ($p = .290$).

Outcome Measures

The efficacy of the weight management program was assessed by measurements of weight and body mass index (BMI). In addition, measurements for the safety of olanzapine and the weight management program were as follows: PANSS, Abnormal Involuntary Movement Scale (AIMS), vital signs (blood pressure, pulse rate), laboratory data including hematology (hemoglobin, hematocrit, erythrocyte count, mean cell volume, leukocyte, platelet count), clinical chemistry (sodium, potassium, total bilirubin, alkaline phosphatase, gamma-glutamyl transferase, AST, ALT, blood urea nitrogen, creatinine, uric acid, glucose, total protein, albumin), lipid profile (cholesterol, low-density lipoprotein [LDL], high-density lipoprotein [HDL], triglyceride), and urinalysis (pH, albumin, glucose, ketones, bilirubin, blood, urobilinogen, white blood cells). We assessed subjects according to the World Health Organization-Quality of Life-Brief version (WHO-QOL-BREF) for health outcomes.[13] The WHO-QOL-BREF, designed to assess quality of life in health and health care, contains

Table 1. Baseline Characteristics of Subjects With Schizophrenia or Schizoaffective Disorder[a]

Variable	Intervention Group (N = 33)	Control Group (N = 15)	p Value
Sex, N[b]			1.000
Male	10	5	
Female	23	10	
Age, y[c]	32.00 ± 9.22	29.80 ± 6.07	.404
Duration of illness, y[c]	2.01 ± 1.09	2.20 ± 1.06	.580
BMI, kg/m^2[c]	26.81 ± 3.85	27.99 ± 3.87	.329
PANSS score[c]	46.76 ± 10.93	47.33 ± 10.20	.864
AIMS score[c]	0.91 ± 1.89	0.80 ± 1.66	.849
Daily dose, mg/d[c]	10.38 ± 5.93	11.33 ± 4.81	.588
WHO-QOL-BREF score[c]	77.61 ± 11.42	75.07 ± 9.35	.455
Pulse rate[d]	77.94 ± 8.01	79.07 ± 5.59	.384
Blood pressure, mm Hg[d]			
Systolic	115.55 ± 9.86	124.07 ± 15.01	.049
Diastolic	74.97 ± 8.06	80.53 ± 10.13	.056

[a]Values are presented as mean ± SD unless otherwise specified.
[b]Fisher exact test was used.
[c]Independent t test was used.
[d]Wilcoxon rank sum test was used.
Abbreviations: AIMS = Abnormal Involuntary Movement Scale, BMI = body mass index, PANSS = Positive and Negative Syndrome Scale, WHO-QOL-BREF = World Health Organization-Quality of Life-Brief version.

Table 2. Contents of the Weight Management Program Applied to Study Subjects With Schizophrenia or Schizoaffective Disorder

Variable	Content
Weight and body mass index	
Diet management	
Food diary	Daily ingestion list
	Food plan
Education about eating behavior improvement	Food exchange table
	Food model
	Importance of regular eating behavior
	Healthy snacking
	Cooking preparation for lowering calories
	Food shopping
	Reading food label
Exercise management	
Exercise diary	Daily activity list
	Exercise plan
Education about daily lifestyle modification	Waist/hip ratio
	Calorie consumption of daily life activity
	Correct aerobic/anaerobic exercise
	Choosing exercise suitable for patient
	Correcting false common sense about diet
	Yo-yo phenomenon
	Using community health center
Safety	Positive and Negative Syndrome Scale
	Abnormal Involuntary Movement Scale
	Vital signs
	Laboratory monitoring
Quality of life	World Health Organization–Quality of Life–Brief version
Compliance	Compliance with drug, diet, and exercise management

26 items and is scored over 4 major domains: physical health, psychological well-being, social relationships, and environment. Domain scores are scaled in a positive direction, higher scores signifying higher quality of life, with the highest possible score being 100. This study also measured the participants' compliance with the exercise and diet program, as well as with the drug treatment.

Study Design

The main components of this study were diet and exercise management, which were based on cognitive and behavioral therapy. Measurements of safety, QOL, and compliance with olanzapine treatment and the weight management program comprised the remainder of the study (Table 2). The weight management program was carried out in an individual format.

Diet management included the keeping of a food diary and nutritional education. A dietician discussed the food diaries with the patients and helped with diet planning at every visit. In addition, subjects were educated about important nutritional concepts, including the food exchange table, using food models, the importance of regular eating behavior, healthy snacking, low-calorie cooking preparation, food shopping, and reading food labels.

Exercise management included the keeping of an exercise diary and education regarding daily lifestyle modifications for weight control. Subjects were urged to keep an exercise diary. An exercise coordinator discussed the exercise diaries with the patients, evaluated their exercise protocols, and helped patients with exercise planning at every visit. The education regarding daily lifestyle modification in the exercise management program included checking waist/hip ratio, explanations of calorie consumption in daily activities, correct aerobic/anaerobic exercise, choosing exercise suitable for the patient, correcting common misconceptions about diet, the "yo-yo phenomenon," and using the community health center.

After a screening evaluation, including a psychiatric evaluation, physical examination, and screening laboratory tests, the participants who fulfilled the inclusion/exclusion criteria were randomly allocated to either the intervention group or the control group. The treatment period was 12 weeks, and all participants continued to take olanzapine (5–20 mg/day). Intervention group patients were also involved in the weight management program, including both diet and exercise management, and during the first 4 weeks of the study, patients visited the clinical center once a week. After the first 4 weeks, patients visited the clinic every other week. Control group patients received the routine care with verbal recommendations as to their physical activity and eating behavior. They visited the clinical center once a month for 12 weeks.

At visit 1, the patients received a physical examination and had their blood pressure, pulse rate, weight, BMI, eating inventory, AIMS, and WHO-QOL-BREF checked. The patients in the intervention group participated in the

weight management program that consisted of education about keeping food and exercise diaries, eating behavior improvement, and lifestyle modification for weight control. The patients in the control group received only food and exercise diaries.

At 4 and 8 weeks, assessment of the patients was performed, including physical examination, blood pressure, pulse rate, weight, BMI, AIMS, and compliance with olanzapine and the weight management program.

At 12 weeks, an evaluation including physical examination, blood pressure, pulse rate, weight, BMI, endpoint laboratory tests, PANSS, eating inventory, AIMS, WHO-QOL-BREF, adverse events, combination drug use, and compliance with olanzapine and the weight management program was performed.

Statistical Analysis

Data regarding weight changes from baseline to endpoint were analyzed for both the intervention and control groups using paired t tests. Differences in weight changes between the 2 groups were analyzed using a t test. In addition, for adjustment of the effects of clinical center, sex, and age, an analysis of covariance (ANCOVA) was carried out, using clinical center, sex, and age as covariates.

In order to compare the demographic data and adverse events between the 2 groups, t test, Fisher exact test, and Wilcoxon rank sum test were carried out. In addition, differences in the changes of laboratory results, blood pressure, pulse rate, and AIMS, PANSS, and WHO-QOL-BREF scores were analyzed from baseline to endpoint between the intervention and the control groups using t tests. The ratio of LDL to HDL in the laboratory results was calculated.

Compliance with each drug, diet management, and exercise management was also analyzed. Compliance was recorded for each visit and reported as mean percentages as follows—compliance with drug: the ratio of the frequency of actually administered drug to the frequency of prescribed drug; compliance with diet: the ratio of the actual caloric intake (kcal) to the prescribed calorie (kcal); and compliance with exercise: the ratio of the actual exercise amounts (kcal) to the prescribed exercise amounts (kcal).

In cases in which complete data regarding weight during 12 weeks were unavailable, last-observation-carried-forward method was used, with the expectation of the analysis of the weight management program effect on weight change. All analyses were 2-tailed, and the significance level was set at $\alpha = .05$.

RESULTS

Weight and BMI Changes

Of the 48 patients enrolled, the data on 5 subjects were incomplete with regard to body weight. Therefore, 43 patients with complete weight change data during the treatment period were included in the analysis of the weight management program effect on weight change (Table 3). Significant differences in weight and BMI change from baseline to endpoint were seen between the intervention group and the control group. Patients in the weight management program exhibited a mean weight reduction of –3.94 ± 3.63 kg compared with –1.48 ± 1.88 kg in the control group (p = .006). In addition, BMI reduction in patients in the weight management program was –1.50 ± 1.34 compared with –0.59 ± 0.73 in the control group (p = .007). In completed cases in which 36 patients (N = 22 in the intervention group and N = 14 in the control group) were included, on the other hand, significant differences in weight and BMI change from baseline to endpoint were also found between the intervention group and the control group (weight change: –5.05 ± 3.50 vs. –1.48 ± 1.88, p < .001; BMI change: –1.92 ± 1.28 vs. –0.59 ± 0.73, p < .001).

Table 3. Weight Change From Baseline to Each Visit in the Intervention and Control Groups[a]

Variable	Intervention Group (N = 29)	Control Group (N = 14)	p Value[b,c]
Weight, kg			
Week 4	–1.50 ± 1.68	–0.55 ± 1.54	.081
Week 8	–2.68 ± 2.71	–0.94 ± 2.06	.040
Week 12	–3.94 ± 3.63	–1.48 ± 1.88	.022
Body mass index (BMI), kg/m^2			
Week 4	–0.58 ± 0.66	–0.22 ± 0.58	.090
Week 8	–1.02 ± 1.01	–0.39 ± 0.81	.051
Week 12	–1.50 ± 1.34	–0.59 ± 0.73	.023

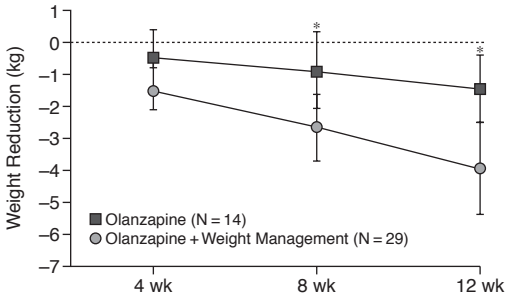
[a]From the last-observation-carried-forward data sheet; group values are means ± SD.
[b]Repeated-measures analysis of variance was used.
[c]Between-groups test: p = .028 (weight), p = .034 (BMI). Interaction-of-time-and-group test: p = .035 (weight), p = .029 (BMI).

In order to examine weight changes at each visit, we applied repeated-measures ANOVA tests to both groups. No significant difference in weight change was detected from baseline to week 4 between the 2 groups. At week 8, significant differences in weight reduction began to appear. With regard to BMI, we found a trend toward differences in BMI reduction between the 2 groups at week 8. At week 12, significant differences in BMI reduction appeared (Table 3 and Figure 1). After adjusting for the effects of sex, age, and clinical site using ANCOVA with sex, age, and clinical site as covariates, significant differences in weight and BMI reduction between the 2 groups were clearly shown (control group: p = .027 vs. weight management group: p = .032).

Measurements for Safety

With respect to the safety results, 48 subjects who enrolled in the study were evaluated in total. For PANSS, AIMS, and vital signs, 39 subjects (intervention group:

Figure 1. Weight Reduction in Subjects During 12-Week Weight Management Program[a]



[a]From the last-observation-carried-forward data sheet. The between-groups test indicated that the difference in weight between groups was significant (p = .028); consequently, the lines for the 2 groups in the graph are rather far apart. The interaction of time and group was significant (p = .035), which means that the groups were changing over time but were changing in different ways; consequently, the lines in the graph are not parallel.
*p < .05.

N = 25 and control group: N = 14) were available, and 38 subjects (intervention group: N = 24 and control group: N = 14) were available for laboratory data analysis.

With respect to psychiatric symptoms (PANSS, AIMS) and adverse events identified as treatment-emergent adverse events, no significant differences were found between the 2 groups at baseline and after treatment. In addition, changes from baseline to endpoint in systolic and diastolic blood pressure and pulse rate in the intervention and the control groups were –1.12 versus 1.36, 4.52 versus 4.00, and –1.80 versus –0.79, respectively. These differences between the 2 groups, however, were not statistically significant. There were no significant differences in any laboratory data between the 2 groups, either before or after treatment. The ratio of LDL to HDL in lipid profile was decreased by 0.19 from 2.91 to 2.72 in the intervention group and by 0.04 from 3.29 to 3.25 in the control group. The ratio was decreased in 17 (70.8%) of 24 patients in the intervention group and 7 (50.0%) of 14 patients in the control group. The number of subjects with decreasing ratio in the intervention group was larger than that in the control group, but the difference was not statistically significant in either the proportions (p = .199) or the change of ratio from baseline (p = .556).

Measurements of Health Outcomes

The total number of patients available for the final health outcomes evaluation with the WHO-QOL-BREF was 39 (N = 25 in the intervention group, N = 14 in the control group). There was a trend toward statistical difference in the physical health score changes between the weight management group and control group (1.12 in the intervention group vs. –0.93 in the control group, p = .067). However, for psychological well-being, social relationship, and environmental domain, the scores did not show a statistically significant difference between the intervention group and control group.

Compliance

Thirty-six patients (N = 22 in the intervention group, N = 14 in the control group) completed this study, although 48 patients (N = 33 in the intervention group, N = 15 in the control group) were initially enrolled. With regard to compliance with olanzapine treatment, 21 (63.6%) of 33 patients in the intervention group and 14 (93.3%) of 15 patients in the control group scored over 80% compliant. Of the 33 patients in the weight management program, all 22 subjects who completed the study were over 80% compliant with diet management, and 12 patients (36.4%) were over 80% compliant with exercise management.

DISCUSSION

This was a prospective study on the efficacy of a weight management program in patients with schizophrenia or schizoaffective disorder taking olanzapine compared with a randomized control group. In this study, patients treated with olanzapine undergoing a 12-week weight management program exhibited significant reductions in weight and BMI compared with patients receiving usual outpatient treatment. In addition, with regard to the safety of olanzapine treatment and the weight management program, no significant differences in PANSS, AIMS, blood pressure, pulse rate, and laboratory data between the intervention group and the control group were observed after treatment.

Although there is no consensus regarding the time course of weight gain during antipsychotic drug treatment, the literature generally indicates that the majority of weight gain occurs during the first 3 months.[14,15] Moreover, Kinon et al.[16] reported that the rate of weight gain in patients with schizophrenia was most rapid during the first 12 weeks of olanzapine treatment, suggesting the importance of early intervention for weight gain in patients undergoing olanzapine treatment. In our present results, patients undergoing a 12-week weight management program incorporating diet and exercise management benefited, experiencing weight reduction of –3.94 ± 3.63 kg. This result suggests that early active intervention may prevent weight gain in patients with schizophrenia who undergo olanzapine treatment.

When a weight management program is applied to patients with schizophrenia, some specific issues must be addressed. Schizophrenic patients may exhibit deficits in attention, motivation, and memory, thereby affecting their ability to benefit from a weight management program.[17] However, some reports have indicated relatively high efficacy with regard to weight control in patients with

schizophrenia.[18–20] Ball et al.[18] evaluated the effectiveness of a Weight Watchers program in patients with schizophrenia who had experienced weight gain during treatment with olanzapine. Although no statistically significant differences in weight change were found between 11 patients and a comparison group, 7 men experienced significant weight loss, suggesting that weight loss strategies may be at least partially successful among such patients. Menza et al.[20] reported on the feasibility and efficacy of a multimodal weight control program for overweight and obese mentally ill adults who gained weight during treatment with atypical antipsychotic medication. According to Menza et al.,[20] patients with schizophrenia or schizoaffective disorder were willing to attend and benefited from a weight control program focusing on nutrition, exercise, and motivation and exhibited reductions in weight and BMI.

Quality of life has recently become an issue of growing interest. The focus of treatment has moved away from the mere attenuation of symptoms and grown to encompass the improvement of subjective and objective aspects related to QOL. Recent research has shown that atypical antipsychotics improved QOL in patients with schizophrenia.[21–23] According to Ritchie et al.,[24] olanzapine treatment, specifically, was associated with a better response as opposed to risperidone on the psychological domain of the WHO-QOL-BREF when switching from conventional antipsychotics to olanzapine or risperidone in elderly patients with schizophrenia. In the present study, patients with schizophrenia who received olanzapine with a weight management program showed increased physical health scores, whereas scores decreased in patients who were without a weight management program. Thus, the weight management program seemed to be effective in physical well-being.

With regard to the present results, it is necessary to note the dropout rate of the patients in the weight management program. Of 48 patients enrolled, 36 patients completed this study. While only 1 patient in the control group dropped out, 11 patients dropped out of the weight management program. One patient in the intervention group was dropped from the study due to an inability to contact the patient at week 1, and 10 patients in the intervention group and 1 in the control group dropped out due to their decision to withdraw consent. Specifically, 3 patients in the intervention group and 1 in the control group had problems related to their work, and 7 patients in the intervention group did not want to keep up the weight management program (9 dropped out before week 4 and 2 at week 8). This may come from the difficulty in maintaining adherence to the weight management program for some patients. We looked into the compliance rates associated with each program. As mentioned above, of the 33 patients enrolled in the weight management program, 22 patients were over 80% compliant with the diet management protocols, but only 12 patients (36.4%) were over 80% compliant with the exercise management protocols. These results indicate that patients experienced more difficulty in exercise management than in diet management. Therefore, it is necessary to adjust the exercise management program to increase the compliance of patients with schizophrenia.

In this study, patients in the control group undergoing usual outpatient treatment also exhibited weight reduction at the completion of the 12-week treatment period. When comparing the ratio of patients exhibiting weight reduction between the 2 groups, no difference was found. That is to say, 25 (86.2%) of 29 patients in the intervention group and 12 (85.7%) of 14 patients in the control group exhibited weight reduction. However, 7 (28.0%) of 25 patients in the intervention group lost more than 10% of their pretreatment body weight, while no patients in the control group did. As this study was a weight control clinical trial and all subjects enrolled in this study knew they were participating in a weight control study, it is likely that the patients allocated to the control group were also hoping to lose weight. Therefore, they may have made efforts to reduce their weight in everyday life aided by the counseling received during the study visits, the so-called "Hawthorne Effect," which states that by merely participating in a study, the participants have a better experience because the focus of interest on them is gratifying and thus rewarding in its own right.

There are some limitations of this study. One is that the sample size was small; thus, more patients should be studied to determine if the results of this study apply to most patients taking antipsychotics. Another limitation of this study involves the duration of treatment. This weight management program was designed for outpatients taking olanzapine for 12 weeks' duration. In a 52-week, multimodal weight control program, Menza et al.[20] reported that the preponderance of weight change in patients on a weight control program who had gained weight while taking atypical antipsychotics occurred over the first 3 months and, thereafter, the reduced weight was maintained. Further study may be necessary to determine the long-term effects of the current weight management program.

CONCLUSIONS

This study suggests that a weight management program may be effective and safe for weight reduction in patients with schizophrenia or schizoaffective disorder during olanzapine treatment. In addition, a weight management program may improve the QOL of patients with schizophrenia, specifically with respect to physical well-being. Clinicians should be aware of the possibility of weight gain when prescribing antipsychotic agents and that early active intervention for weight control may also provide patients with enhanced QOL.

Drug names: clozapine (Clozaril, FazaClo, and others), olanzapine (Zyprexa), risperidone (Risperdal), ziprasidone (Geodon).

REFERENCES

1. Allison DB, Fontaine KR, Manson JE, et al. Annual deaths attributable to obesity in the United States. JAMA 1999;282:1530–1538
2. Must A, Spadano J, Coakley EH, et al. The disease burden associated with overweight and obesity. JAMA 1999;282:1523–1529
3. Weiden PJ, Mackell JA, McDonnell DD. Obesity as a risk factor for antipsychotic noncompliance. Schizophr Res 2004;66:51–57
4. Allison DB, Mentore JL, Heo M, et al. Antipsychotic-induced weight gain: a comprehensive research synthesis. Am J Psychiatry 1999;156:1686–1696
5. Ganguli R. Weight gain associated with antipsychotic drugs. J Clin Psychiatry 1999;60(suppl 21):20–24
6. Wirshing DA, Wirshing WC, Kysar L, et al. Novel antipsychotics: comparison of weight gain liabilities. J Clin Psychiatry 1999;60:358–363
7. Bobes J, Rejas J, Garcia-Garcia M, et al. Weight gain in patients with schizophrenia treated with risperidone, olanzapine, quetiapine or haloperidol: results of the EIRE study. Schizophr Res 2003;62:77–88
8. Arato M, O'Connor R, Meltzer HY. A 1-year, double-blind, placebo-controlled trial of ziprasidone 40, 80 and 160 mg/day in chronic schizophrenia: the Ziprasidone Extended Use in Schizophrenia (ZEUS) study. Int Clin Psychopharmacol 2002;17:207–215
9. Bagri S, Reddy G. Delirium with manic symptoms induced by diet pills [letter]. J Clin Psychiatry 1998;59:83
10. Cleare AJ. Phentermine, psychosis, and family history [letter]. J Clin Psychopharmacol 1996;16:470–471
11. Faulkner G, Soundy AA, Lloyd K. Schizophrenia and weight management: a systematic review of interventions to control weight. Acta Psychiatr Scand 2003;108:324–332
12. National Heart, Lung, and Blood Institute (NHLBI). Obesity Education Initiative Expert Panel on the Identification, Evaluation, and Treatment of Overweight and Obesity in Adults. Clinical Guidelines on the Identification, Evaluation, and Treatment of Overweight and Obesity in Adults: The Evidence Report. Bethesda, Md: National Heart, Lung, and Blood Institute; 1998
13. World Health Organization. WHO-QOL-BREF Introduction, Administration, Scoring and Generic Version of the Assessment. Geneva, Switzerland: World Health Organization; 1996
14. Lamberti JS, Bellnier T, Schwarzkopf SB. Weight gain among schizophrenic patients treated with clozapine. Am J Psychiatry 1992;149: 689–690
15. Hummer M, Kemmler G, Kurz M, et al. Weight gain induced by clozapine. Eur Neuropsychopharmacol 1995;5:437–440
16. Kinon BJ, Basson BR, Gilmore JA, et al. Long-term olanzapine treatment: weight change and weight-related health factors in schizophrenia. J Clin Psychiatry 2001;62:92–100
17. Elvevag B, Goldberg TE. Cognitive impairment in schizophrenia is the core of the disorder. Crit Rev Neurobiol 2000;14:1–21
18. Ball MP, Coons VB, Buchanan RW. A program for treating olanzapine-related weight gain. Psychiatr Serv 2001;52:967–969
19. Umbricht D, Flury H, Bridler R. Cognitive behavior therapy for weight gain [letter]. Am J Psychiatry 2001;158:971
20. Menza M, Vreeland B, Minsky S, et al. Managing atypical antipsychotic-associated weight gain: 12-month data on a multimodal weight control program. J Clin Psychiatry 2004;65:471–477
21. Franz M, Lis S, Pluddemann K, et al. Conventional versus atypical neuroleptics: subjective quality of life in schizophrenic patients. Br J Psychiatry 1997;170:422–425
22. Hamilton SH, Revicki DA, Genduso LA, et al. Olanzapine versus placebo and haloperidol: quality of life and efficacy results of a North American double-blind trial. Neuropsychopharmacology 1998;18:41–49
23. Montes JM, Ciudad A, Gascon J, et al., for the EFESO Study Group. Safety, effectiveness, and quality of life of olanzapine in first-episode schizophrenia: a naturalistic study. Prog Neuropsychopharmacol Biol Psychiatry 2003;27:667–674
24. Ritchie CW, Chiu E, Harrigan S, et al. The impact upon extra-pyramidal side effects, clinical symptoms and quality of life of a switch from conventional to atypical antipsychotics (risperidone or olanzapine) in elderly patients with schizophrenia. Int J Geriatr Psychiatry 2003; 18:432–440