Management of Weight Gain in Patients With Schizophrenia

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Of the roughly 55% of the United States population that is considered overweight, half meet the criteria for obesity. Obesity is associated with serious health risks, but many clinicians graduate from medical school without a clear understanding of the effects of the foods that they and their patients consume. Obesity is more prevalent in people with mental illnesses, which poses an even greater challenge to clinicians. Antipsychotic treatment can cause weight gain, and mentally ill patients generally lack an understanding of nutrition as well as the ability to afford healthier foods. Therefore, clinicians must educate themselves about appropriate measures for preventing weight gain before or immediately after initiating antipsychotic therapy. Strategies for weight gain management that have proven effective in clinical trials include regular check-ups, lifestyle and medication counseling, medication assessments, behavioral control programs, and pharmacologic intervention. These approaches are necessary for clinicians to consider if efforts at reintegration of mentally ill patients are to succeed.
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Managing weight gain in patients with schizophrenia, who have a high prevalence of obesity[1] or who may be at risk for gaining weight due to antipsychotic treatment,[2] is difficult but not impossible. Several strategies exist for controlling and decreasing the weight of these patients. Given the health consequences of obesity, clinicians should implement these strategies before, or as soon as, patients show signs of weight gain.

PREVALENCE AND IMPACT OF OBESITY

In the United States, roughly 55% of adults are overweight.[3] Half of those people, meaning 1 in 4 Americans, actually meet the criteria for obesity. According to the National Heart, Lung, and Blood Institute (NHLBI)[4] of the National Institutes of Health (NIH), overweight is classified as a body mass index (BMI) of 25 to 29.9 kg/m^2 and obesity is a BMI greater than 30 kg/m^2. There are 3 classes of obesity as defined by the NHLBI (Table 1).

Groups disproportionately affected or at risk for obesity are the poor, minority populations,[5] especially African-American women, and children and/or adolescents.[5,6] Obesity is inversely associated with social class,[7] possibly because high fat content foods are less expensive than healthier foods. It is much less clear why obesity is more prevalent in African American women and in children and adolescents. Some possible explanations for childhood obesity include less physical activity and more time spent in front of the television or computer, greater access to fast food, and less access to healthy food because dual-income families have less time to prepare home-cooked meals.[6] The traditional African American diet remains high in saturated fat, calories, and protein, and an African American cultural tradition is frequent family gatherings that include regular feasting. Statistically, African American women tend to have more financial challenges than Caucasian women so are less likely to spend money on exercise and weight loss, and studies show that African American women appear to have a slower metabolism than Caucasian women.[8–10] Hopefully, more research on obesity will provide other explanations as to why these groups are at high risk, as well as solutions to the problem.

As weight increases, so too does the impact of the excess weight on all organ systems, raising the incidences of morbidity and mortality. Consequently, obesity is a major cause of mortality in the United States; it is the second leading cause of preventable death after smoking.[6] In addition, a number of medical disease states, such as hypertension, dyslipidemia, diabetes mellitus, and coronary artery disease, are adversely impacted by obesity (Table 2).[3] Estimates of the direct and indirect costs of obesity in the United States amount to almost $100 billion annually.[11]

CAUSES OF OBESITY

Obesity in Patients With Mental Illness

Clinicians continue to struggle with the causes of obesity, particularly for people with serious and persistent mental illness. Data show that obesity can be 2 to 3 times more prevalent in people with serious mental illness than in the general population.[1] Weight gain may represent, in part, recovery from a disease-associated weight loss. For example, many patients with schizophrenia have been homeless or have had serious mental illness for many years and have not been in supervised or supportive environments. This particular group of patients experiences weight gain because of the stability and the routine of having 3 meals provided in the course of a day.

Unfortunately, in medical school, there is little emphasis on nutrition education. Many clinicians, particularly in the United

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Table 1. Classification of Overweight and Obesity by BMI[a]

Classification	BMI (kg/m^2)
Underweight	< 18.5
Normal	18.5–24.9
Overweight	25.0–29.9
Obesity	
Class I	30.0–34.9
Class II	35.0–39.9
Extreme obesity	
Class III	≥ 40

[a]Data from NHLBI.[3] Abbreviation: BMI = body mass index.

Table 2. Illnesses and Complications Impacted by Obesity

Hypertension
Dyslipidemia
Diabetes mellitus
Coronary artery disease
Congestive heart failure
Stroke
Osteoarthritis
Gallstones
Cancers (endometrial, gallbladder, colon, breast)
Menstrual abnormalities
Pregnancy risks
Impaired fertility

Table 3. Estimated Weight Gain After 10 Weeks of Antipsychotic Treatment[a]

Drug	kg	lb
Haloperidol	0.5	1.1
Risperidone	2.0	4.4
Chlorpromazine	2.1	4.7
Sertindole	2.9	6.4
Olanzapine	3.5	7.8
Thioridazine	3.5	7.8
Clozapine	4.0	8.9
Ziprasidone	0.04	0.09

[a]Data from Allison et al.[2]

States, graduate without having a clear understanding of the effects of the foods that they and their patients consume. For example, a cheeseburger with sauce, as sold in fast food chains, can contain as many as 770 calories. Bologna, American cheese, and mayonnaise on a roll can contain as many as 750 calories. A large bag of potato chips, which costs as little as $0.99, contains 8 servings at 220 calories per serving for a total of 1760 calories per bag. A 24 oz soda contains about 360 calories and costs less than $1.00.

Clinicians with practices in residential settings are able to observe patients at all times of the day. In such a setting it is extremely common to see many patients with extra money buying a number of these high-calorie food items in the afternoon, after having already consumed 2000 calories in the course of a day. Thus, these patients are adding another 2000 to 2500 calories to their diet for a daily total consumption of as much as 4500 calories. This first-hand experience, in addition to evidence in the medical literature, indicates that increased caloric intake seems to be a factor contributing to weight gain.

Obesity in Patients Taking Antipsychotics

Weight gain has also been reported during treatment with conventional and atypical antipsychotic agents, but several studies have shown little difference in weight gain potential among antipsychotics. A retrospective study by Allison et al.[2] estimated the average weight gained by patients treated with various antipsychotic medications (Table 3). They reported that haloperidol and ziprasidone caused less weight gain when compared with the other antipsychotics but found little difference in weight gain among the other antipsychotics. Another study[12] comparing weight change with olanzapine, haloperidol, and risperidone showed a significant increase in weight with olanzapine compared with haloperidol, but no significant difference in weight gain between olanzapine and risperidone.

The effects on weight of long-term treatment with antipsychotics have also been examined. A retrospective analysis[13] of long-term olanzapine treatment examined 573 patients receiving olanzapine 5 to 20 mg/day and 103 patients receiving haloperidol 5 to 20 mg/day for 39 weeks or more. Of the 573 patients taking olanzapine, 293 were observed for between 2.5 and 3 years, with 147 observed at the final 3-year timepoint. Of the 103 patients taking haloperidol, the maximum time observed was 100 weeks (1.9 years). As shown in Figure 1, 26% of olanzapine-treated patients lost weight or gained no weight, 44% gained > 0 to 10 kg (0–22 lb), 22% gained > 10 to 20 kg (22–45 lb), and 9% gained > 20 kg (45 lb). For haloperidol, 47% lost weight or gained no weight, 44% gained > 0 to 10 kg (0–22 lb), 9% gained > 10 to 20 kg (22–45 lb), and 3% gained more than 20 kg (45 lb). Fifty-two percent of olanzapine-treated patients gained > 7% of their body weight, compared with 26% of haloperidol-treated patients. Patients with the lowest baseline BMI had the greatest weight gain, and maintenance dose was not a predictor of weight change.

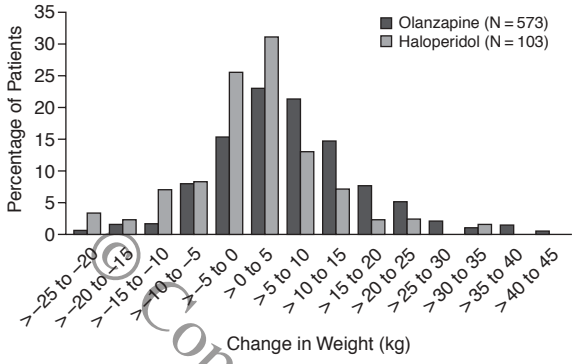
In a study by Tran et al,[14] 78% of olanzapine-treated patients gained < 10 kg (22 lb), and 20% gained > 10 kg (22 lb). For the risperidone group, 88.0% gained < 10 kg (22 lb), and 8.6% gained > 10 kg (22 lb) (Figure 2).[15] A total of 339 patients (olanzapine N = 172, risperidone N = 167) were assigned to receive double-blind therapy, and 178 patients (52.5%) completed the study.[14] After 28 weeks, the mean weight gains were 4.1 ± 5.9 kg (9.1 ± 13.1 lb) in the olanzapine group and 2.3 ± 4.8 kg (5.1 ± 10.7 lb) in the risperidone group. Most patients reached a plateau by 6 months. Again, those patients with the lowest baseline BMI showed the greatest amounts of weight gain.

Although dose does not appear to correlate with weight gain in antipsychotic treatment,[11] some evidence shows that weight gain during atypical antipsychotic treatment, like weight gain in general, may be predicted by increased appetite, lower baseline BMI, gender, and age.[4,11] Although further study is necessary to confirm these associations, overweight patients should not be excluded from atypical antipsychotic therapy.

STRATEGIES FOR MANAGING WEIGHT GAIN

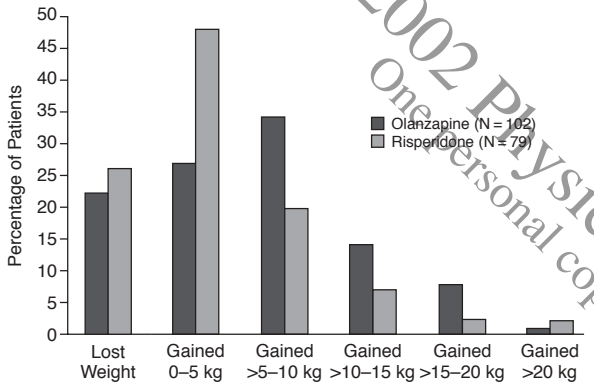
Weight gain in mentally ill patients is an evident problem, so clinicians need to adopt appropriate measures to prevent weight gain before or immediately after initiating antipsychotic therapy. As well as counseling patients about the expected benefits of antipsychotic treatment, clinicians should also counsel patients about the potential for an increase in appetite as a result of treatment. Patients should be weighed at baseline, prior to starting antipsychotic medication, and at every visit or regularly thereafter. Physicians should encourage lifestyle changes that will help patients control their weight (Table 4). It is well known that smoking cessation is often associated with weight gain. Therefore, a patient that stops smoking after an improvement in cognitive function, which occurs as a result of treatment with antipsychotics, has a greater potential for weight gain. Clinicians can encourage patients to be careful when choosing foods and educate patients about alternatives to foods high in saturated fats.

Figure 1. Weight Changes Among Olanzapine Versus Haloperidol Patients Observed After ≥ 39 Weeks[a]



[a]Reprinted from Kinon et al.[13] with permission.

Figure 2. Weight Changes Among Olanzapine Versus Risperidone Patients at Endpoint[a]



[a]Reprinted from Jones et al.[15] with permission.

Clinicians have several strategies to choose from for weight gain management. First, the level of medication response versus the overall safety profile of a patient's medications should be assessed. A medication assessment should include all current medications that may contribute to weight gain. Many medications other than antipsychotics, such as mood stabilizers like valproate and antihypertensive agents, can cause weight gain.[1,16] After reviewing a patient's medications, clinicians should be able to determine what impact, if any, the medications are having on weight gain and modify the regimen, if possible.

An intensive effort to modify daily caloric intake is one of the most important and beneficial intervention tools. Although behavioral controls have met with limited success in long-term weight management, they are probably the most useful interventions available to clinicians. In one study,[17] a comprehensive intervention strategy was designed to address issues of overall health, nutrition, and other supportive care including weight reduction support for patients assigned to clozapine, olanzapine, or risperidone. All patients were previously homeless and subject to erratic and nutritionally poor eating. Patients were provided a low-fat, low-calorie diet (average = 2000 calories) with

Table 4. Essential Points of Weight Loss Intervention

Frequent monitoring
Nutritional and lifestyle counseling
Skills training that focuses on exercise, diet, health education, and behavioral techniques

Table 5. Body Weight Profile of Patients During Atypical Antipsychotic Treatment Before and After Behavioral Intervention[a]

Profile	Before Intervention (N = 31)	1 Year After Intervention (N = 31)	1.5 Years After Intervention (N = 28)
Body weight, mean ± SD, lb (kg)	196.8 ± 45.8 (88.6 ± 20.6)	195.5 ± 45.2 (88.0 ± 20.3)	197.7 ± 43.0 (89.0 ± 19.3)
Patients with weight gain, N (%)	19 (61)	10 (32)	12 (43)
Percent change in body weight, mean ± SD	...	0.46 ± 6.59	0.28 ± 8.49

[a]Reprinted from Aquila and Emanuel[17] with permission.

increased fresh produce. Portion size was decreased for all foods, except vegetables and lettuce and/or salad, and servings were limited to one per person. Support groups were formed for weight reduction, and a group was initiated by the nutritionist to educate patients about proper eating habits and consequences of nutrition on physical health. At the start of the study, 19 (61%) of 31 patients showed weight gain (Table 5). In contrast, 1 year after intervention, only 10 (32%) of 31 patients had gained weight, and there was no statistically significant difference in mean body weight on the new management regimen. After 18 months, 12 (43%) of 28 patients had increasing body weight, again with no difference in mean body weight over time. The percent change in body weight was not statistically significant at either time point after study intervention. Effects were similar regardless of medication.

A study by Wirshing et al.[18] included a behavioral intervention in which patients were referred to a wellness clinic where dietary and exercise habits were evaluated and exercise classes and support groups were available. The subjects were 92 male patients who were participants in 8 different clinical drug trials conducted over 6 years. One study compared clozapine with haloperidol, 2 compared risperidone with haloperidol, 1 compared sertindole with placebo, 1 compared 4 dose levels of haloperidol decanoate, and 1 compared olanzapine with risperidone. All patients were instructed to weigh themselves and report their weight to the nurse at each visit (every 1 to 4 weeks). A gain of 10 lb (4.5 kg) was considered sufficient to warrant further intervention, and those patients were instructed to keep a detailed diary of all food intake over a several week period. If this failed to maintain or decrease weight, they were then referred to a clinic that provided a more rigorous evaluation of dietary and exercise habits, education, exercise classes, and group support. During the study, 12 patients lost weight, and for all groups, final weight gain was lower than maximum weight gain (Table 6).

Another behavioral intervention being studied is Weight Watchers®. It has been one of the more successful modalities for treatment of overweight and obesity in the general population,

Table 6. Beginning Weight and Maximum and Final Weight Gain During Antipsychotic Treatment With Behavioral Intervention[a]

Variable	Drug				
	Clozapine	Olanzapine	Risperidone	Haloperidol	Sertindole
Beginning weight, mean ± SD					
lb	184.4 ± 33.5	190.0 ± 43.6	185.6 ± 38.0	186.0 ± 36.2	188.8 ± 30.1
kg	83.0 ± 15.1	85.5 ± 19.6	83.5 ± 17.1	83.7 ± 16.3	84.9 ± 13.5
Maximum weight gain, mean ± SD					
lb	16.8 ± 13.3	17.8 ± 13.3	9.1 ± 7.6	7.7 ± 9.0	5.6 ± 7.3
kg	7.5 ± 6.0`	8.0 ± 6.0	4.1 ± 3.4	3.5 ± 4.1	2.5 ± 3.3
Maximum % weight gain, mean ± SD	9.5 ± 8.1	10.5 ± 10.3	5.2 ± 4.4	4.1 ± 4.7	3.2 ± 4.5
Final weight gain, mean ± SD					
lb	14.1 ± 13.5	6.2 ± 14.1	4.2 ± 9.2	3.0 ± 10.9	0.5 ± 8.6
kg	6.3 ± 6.1	2.8 ± 6.4	1.9 ± 4.2	1.4 ± 4.9	0.2 ± 3.9
Final % weight gain, mean ± SD	8.0 ± 8.2	4.2 ± 9.8	2.5 ± 5.3	1.6 ± 5.7	0.6 ± 5.2

[a]Adapted from Wirshing et al.[18]

and a number of clinicians are beginning to implement it. Preliminary data for a study that is currently underway show a 5 lb (2.25 kg) to 10 lb (4.5 kg) average weight loss for patients enrolled in the Weight Watchers® group.[19]

If psychosocial strategies fail to produce adequate results, recent studies have shown success with pharmacologic interventions for weight gain management. Floris et al.[20] studied the addition of amantadine at 100 q.d., 100 b.i.d., and 100 t.i.d. to a small group of patients being treated with olanzapine who had already gained weight. Results of the study showed an average weight loss of 3.5 kg (7.8 lb). These observations of successful post–weight-gain intervention merit confirmation in randomized, controlled trials. Another pharmacologic intervention is the implementation of H_2 antagonists with antipsychotic treatment. A 16-week, randomized, double-blind, placebo-controlled, open-label study[21] showed that patients treated with nizatidine, 300 mg b.i.d., added to olanzapine treatment, gained an average of 2.5 kg (5.6 lb) compared with the 5.5 kg (12.2 lb) gained by patients treated with only olanzapine. However, this modality has only been successful prior to any weight gain.

SUMMARY

Weight gain is clinically manageable in most patients and seems to be similar for all antipsychotic treatments. Therefore, clinicians need to implement weight management strategies when initiating treatment, and be aware of any increases in appetite after beginning treatment. Strategies should include nutritional education, which is essential for managing weight gain, and patients should be encouraged to participate in an exercise program. Data suggest that both behavioral and adjunctive pharmacologic strategies can halt or reduce weight gain. These approaches are necessary for clinicians to consider if efforts at reintegration of the mentally ill patient are to succeed.

Drug names: amantadine (Symmetrel and others), chlorpromazine (Thorazine and others), clozapine (Clozaril and others), haloperidol (Haldol and others), nizatidine (Axid), olanzapine (Zyprexa), risperidone (Risperdal), ziprasidone (Geodon).

Disclosure of off-label usage: The author has determined that, to the best of his knowledge, no investigational information about pharmaceutical agents has been presented in this article that is outside U.S. Food and Drug Administration–approved labeling.

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