Weight Gain With Risperidone Among Patients With Mental Retardation: Effect of Calorie Restriction

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Background: The atypical antipsychotics cause weight gain, which is poorly understood in terms of its mechanism and treatment. A usual recommendation for treatment of antipsychotic-induced weight gain includes calorie restriction and exercise. The authors describe their recent clinical experience with calorie restriction in adults with mental retardation treated with risperidone.

Method: A retrospective chart review was performed on the records of 50 adult patients with mental retardation treated with risperidone while residing at a habilitation center. We assessed dose and duration of risperidone treatment, weight, changes in calorie intake, and frequency of aggressive behavior.

Results: Of the 50 patients, 39 had adequate data for analysis. Thirty-seven of the 39 patients gained weight with a mean of 18.8 lb (8.3 kg) over about 2 years. Twenty of the 37 patients were calorie restricted. Three of the 20 calorie-restricted patients lost weight at a rate of 0.2 lb (0.1 kg) per month. The other 17 calorie-restricted patients and the 17 patients who were not calorie restricted continued to gain weight at a rate of 0.8 lb (0.4 kg) per month over about another 2 years of treatment. The amount of weight gain was not dose related. Calorie restriction led to no deterioration in behavior.

Conclusion: The current investigation lends support to data that note weight gain with risperidone in adults with mental retardation. It suggests that calorie restriction does not lead to weight loss or behavioral deterioration and that weight gain is not dose related.

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The past decade has brought 4 new antipsychotics, considered to be atypical, that hold several advantages over the typical agents such as a reduced likelihood of causing extrapyramidal symptoms and tardive dyskinesia.[1] However, it is now becoming clear that they have their own adverse effects with a growing focus on issues of weight gain, hypertriglyceridemia, and type II diabetes.[2] The mechanism leading to these problems is unclear but may be related to the different receptor binding profiles of these medications.

We have found the atypical antipsychotics, particularly risperidone, to be unusually efficacious in reducing aggression, self-injury, and property destruction in adults with mental retardation.[3] This effect may also be a result of the unique receptor binding profile. The risk/benefit ratio regarding efficacy compared with weight gain and associated risks are not well established in this population of patients.

The usual clinical response to the side effect of weight gain is to recommend vigorous exercise and calorie restriction.[4] Yet, no data document that this approach leads to weight loss, whether one is treating a population with mental retardation or psychotic patients with normal intelligence. Also of concern is the unanswered question as to whether calorie restriction may lead to behavioral deterioration in individuals with severe or profound mental retardation. Lastly, clinicians commonly respond to weight gain by lowering dose of medication with the assumption that the side effect is dose related. Such a dose-response relationship has not been established with risperidone and weight gain. Thus, appropriate clinical response to this problem remains elusive.

We conducted a retrospective study in adults with mental retardation and aggressive behaviors in an attempt to determine the frequency and amount of weight gain associated with risperidone treatment, the effect of calorie restriction on the weight gain and maladaptive behavior, and the relationship between risperidone dose and amount of weight gain.

METHOD

The present study consisted of a chart review of patients treated with risperidone between 1994 and 1999 at Fircrest, a residential habilitation center for adults with mental retardation located in the greater Seattle, Wash.,

Table 1. Mean Rate of Weight Change and Calorie Restriction for 39 Patients With Mental Retardation While Receiving Risperidone Between 1994 and 1999

Calorie Restriction	N	Mean Calories Restricted per Day	Mean Duration of Follow-Up, mo	Mean Weight Change Over Duration, lb (kg)	Mean Rate of Weight Change per Month, lb (kg)
For those placed on calorie restriction					
Gained weight	17	788.2	26.6	21.1 (9.6)	0.8 (0.4)
Lost weight	3	866.7	21.3	–3.7 (–1.7)	–0.2 (–0.1)
For those not placed on calorie restriction					
Gained weight	17	0.0	25.3	20.4 (9.3)	0.8 (0.4)
No weight change	2	0.0	25.3	0.0 (0.0)	0.0 (0.0)

area. In a sample of 306 patients, 50 were treated with risperidone. Thirty-nine of these 50 patients' charts had adequate data for this analysis.

We specifically assessed dose and duration of risperidone treatment, weight (evaluated monthly), changes in calorie intake, and frequency of aggressive behaviors. A majority of these patients had severe or profound mental retardation (IQ < 30) and were unable to complete complex tasks such as regulation of their dietary intake and physical activity.

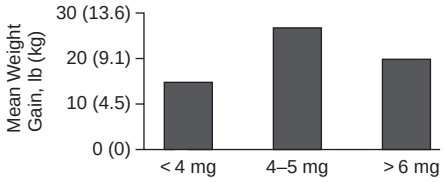
RESULTS

Among the 39 patients, 37 (94.9%) gained weight during therapy with risperidone. The mean weight gain was 18.8 lb (8.3 kg) over a period of 25.6 months of treatment (range, 1–40 lb [0.5–18 kg]). The mean weight gain per month was 0.73 lb (0.33 kg). At the beginning of therapy, all 39 patients had a weight within the ideal body weight range noted by the dietary department of Fircrest.

Following this course of therapy, risperidone treatment was continued, and over half of the patients who gained weight (20/37) were put on calorie restrictions by their primary physician. Before calorie restriction, each patient received a diet consisting of 2400 cal/day. The mean reduction in calorie intake was 800 cal/day (range, 200–1500 cal/day). Meals were delivered by the dietary department and at the order of the attending physician; intake was reduced as ordered. Patients had no other access to food from any other source; therefore, patients could not circumvent the prescribed calorie intake: in light of the severity of their mental retardation, they had no independent means to access food outside that provided by the institution, and the staff did not allow for any calorie intake outside of that delivered by the dietary department. The patients' activity level was not changed. We reviewed weight among these 37 patients over about the next 2 years.

Among the 20 patients who were calorie restricted, 3 (15%) lost some weight (mean of 3.7 lb [1.7 kg] over a period of 21.3 months). The other 17 continued to gain weight at the rate 0.8 lb [0.4 kg] per month (mean of 21.1 lb [9.6 kg] over 26.6 months). The degree of calorie restriction was similar among those who lost weight (866 cal/day) and those who gained weight (788 cal/day). Among the 17 patients who were not calorie restricted, weight gain continued at the rate of 0.8 lb (0.4 kg) per month (Table 1).

Figure. 1. Mean Weight Gain Over a Mean of 25.6 Months Compared With the Daily Dose of Risperidone for 39 Patients



No obvious patterns were noticed between amount of weight gain and dose of risperidone. Mean weight gain was 14.9 lb (6.7 kg) among those treated with less than 4 mg/day of risperidone, 27.2 lb (12.2 kg) among those treated with 4 or 5 mg/day, and 20.2 lb (9.2 kg) among those treated with 6 or more mg/day (Figure 1).

Calorie restriction was not associated with increased frequency of aggressive behaviors.

DISCUSSION

The current study reports the results of a retrospective chart review of 39 patients with mental retardation and aggressive behaviors who were treated with risperidone. We found weight gain to be almost universal in this population (94.9%) with a mean of 18.8 lb (8.3 kg) gained over about a 2-year period of time. We also found the effect of calorie restriction over the next 2 years of treatment to be negligible, as only 15% of patients calorie restricted lost weight and did so at a rate of 0.2 lb (0.1 kg) per month. The remainder of those calorie restricted (85%) as well as those not calorie restricted continued to gain weight at a rate of 0.8 lb (0.4 kg) per month. The amount of weight gain was not dose related, and calorie restriction did not lead to behavioral deterioration.

Our data are consistent with the growing literature that notes weight gain with the atypical antipsychotics in general[5] as well as in the population with mental retardation specifically.[6] Hellings et al.[6] reported an average of 6 lb (2.7 kg) of weight gain in adults with mental retardation

treated with 3 to 4 mg of risperidone for 1 month, and weight gain at 1 year of treatment was twice that seen at 6 months. They suggested that dietary intervention and exercise programming to reduce weight gain merit study. Such nonpharmacologic management of weight gain is the usual recommendation[4] and is consistent with general ideas regarding good health. However, data noting the effectiveness of such a treatment approach are lacking, and our data suggest that in an adult population with mental retardation, calorie restriction is of limited benefit in reversing the weight gain caused by risperidone. We did not alter patient activity level during the course of this roughly 2-year period of treatment. Although regular exercise is an accepted part of good health maintenance, it is not a practical consideration in this population with severe or profound mental retardation whose cognitive impairments preclude such participation.

The lack of benefit noted with our approach to calorie restriction suggests that it is necessary to better understand the mechanism behind the weight gain seen with risperidone in this population. We do not have an explanation for the continued weight gain in spite of significant calorie restriction in our population. The suggestion has been made that the serotonin-2C and histamine-1 receptors may be involved in weight changes with medications.[7] The possible utility of the 2 appetite suppressants approved by the U.S. Food and Drug Administration for the treatment of obesity, sibutramine and orlistat, as well as others not approved for this use yet that have possible weight loss properties, such as topiramate, in bringing about weight loss in adults with mental retardation and weight gain from risperidone remains unknown.

This is a preliminary report with a retrospective chart review design. Our results suggest that risperidone in adults with mental retardation brings significant weight gain and that the mechanism and treatment are poorly understood and require further study.

Drug names: orlistat (Xenical), risperidone (Risperdal), sibutramine (Meridia), topiramate (Topamax).

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