No Weight Gain Among Elderly Schizophrenia Patients After 1 Year of Risperidone Treatment

Yoram Barak, M.D.

Objective: Weight gain has been reported in younger patients treated with most atypical neuroleptics. The goal of this study was to examine whether elderly schizophrenic patients gain weight while being treated with risperidone.

Method: Data are from an international multicenter, open-label study of 180 elderly (69 men, 111 women), chronically ill, psychotic patients (meeting DSM-III-R criteria for schizophrenia or schizophreniform disorder; median age = 72 years [range, 54–89 years]), 97 of whom completed the 12-month study. At endpoint, the mean dose of risperidone was 3.7 mg/day. Patients were weighed at baseline and at endpoint.

Results: There was no significant weight gain in patients who completed the trial (N = 96) or in those who did not complete the entire trial (N = 31).

Conclusion: The results suggest that risperidone treatment is not associated with weight gain among elderly persons with chronic psychosis.

(J Clin Psychiatry 2002;63:117–119)

Received April 5, 2001; accepted July 31, 2001. From the Abarbanel Mental Health Center, Bat-Yam, and the Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel.

The original international multicenter trial from which the data reported in this study came was supported by the Janssen Research Foundation, Beerse, Belgium.

Presented in part at the 7th World Congress of Biological Psychiatry, July 1–6, 2001, Berlin, Germany.

The author thanks Prof. M. Davidson, M.D., and Prof. J. Rabinowitz, Ph.D., for their help with statistical computations and editing.

Corresponding author and reprints: Yoram Barak, M.D., Psychogeriatric Department, Abarbanel Mental Health Center, 15 KKL St., Bat-Yam, 59100, Israel (e-mail: mdybarak@netvision.net.il).

Obesity adversely affects health, especially in elderly persons suffering from diabetes mellitus, hypertension, and cardiovascular disease.[1,2] Patients suffering from schizophrenia, especially elderly patients, are at an increased risk for obesity-related conditions.[3] Thus, antipsychotic-induced weight gain is of particular importance in elderly schizophrenic patients. Despite the availability of a range of studies and meta-analyses[4] establishing that treatment with conventional and atypical antipsychotic agents is associated with antipsychotic-induced weight gain, there is a paucity of research on the association of age and such weight gain. The recently published comparison of distribution of body mass index (BMI) among patients suffering from schizophrenia with that among controls[5] used age-adjusted estimates to conclude that antipsychotic-induced weight gain is an important health concern for many individuals suffering from schizophrenia.

In recent years, there have been many reports on the use of atypical antipsychotics in elderly schizophrenic patients (for review, see Lacro et al.[6]), and there is a growing body of evidence that encourages the use of atypical antipsychotics in elderly schizophrenic patients.[7,8] The aim of the present study was to examine the effects of risperidone on weight gain in elderly schizophrenic patients treated for 12 months.

METHOD

The full details of this study are reported elsewhere.[9] Briefly, this international multicenter, open-label trial examined the efficacy and safety of risperidone when administered for 12 months to 180 elderly psychotic patients, 170 (94%) of whom were diagnosed as having schizophrenia and 10 patients (6%), as having schizophreniform disorder (DSM-III-R). The study enrolled elderly, chronically ill men (N = 69) and women (N = 111) (median age = 72 years [range, 55–89 years]), 97 of whom completed the 12-month study. Of the 180 patients recruited, only 1 was 55 years old and only 4 were aged 60 to 64 years. Thus, 175 patients (97%) were 65 years or older. Weight data were available for 96 of 97 completers and for 31 of the 80 patients who dropped out or discontinued. The most common reasons for discontinuing treatment were adverse experiences (N = 30) and insufficient response (N = 26).

At endpoint, the mean dose of risperidone was 3.7 mg/day. Informed written consent was obtained, and the study was approved by the institutional review board at each participating center.

Patients were weighed at baseline and at the end of the trial. Analyzing change in weight was one of the planned features of the study. The great majority of patients (92%) were long-stay inpatients throughout the study period.[9]

Table 1. Weight at Baseline and Endpoint for Elderly Patients Treated With Risperidone[a]

Patient Group	Baseline	Endpoint
All patients (N = 127)		
Mean ± SD	67.8 ± 13.5 (150.7 ± 30.0)	67.9 ± 13.2 (150.9 ± 29.3)
Median	67 (149)	66 (147)
Range	35.5–111.0 (78.9–246.7)	36.0–113.0 (80.0–251.1)
Completed 12-month study (N = 96)		
Mean ± SD	69.2 ± 13.4 (153.8 ± 29.8)	69.6 ± 13.1* (154.7 ± 29.1)
Median	69.1 (153.6)	68.2 (151.6)
Range	42.5–111.0 (94.4–246.7)	46.0–113.0 (102.2–251.1)
Dropped out/discontinued (N = 31)		
Mean ± SD	63.5 ± 12.9 (141.1 ± 28.7)	62.9 ± 12.3† (139.8 ± 27.3)
Median	64.5 (143.3)	62.2 (138.2)
Range	35.5–88.0 (78.8–195.6)	36.0–97.0 (80.0–215.6)

[a]All values shown as kg (lb). Paired-samples t tests were used for statistical comparisons.
*t = –0.63, df = 95, p = .55, mean difference = 0.37 (95% CI: –1.5 to 0.79).
†t = 1.12, df = 30, p = .27; mean difference = –0.71 (95% CI: –0.58 to 2.00).

All participating centers were university affiliated, practicing in accordance with accepted guidelines. However, no specific or special measures were used or recommended during the trial to prevent weight gain. Data were analyzed using repeated-measures analysis of variance, comparing weight at baseline and weight at endpoint while examining possible differences between men and women and between those who completed the entire trial and those who did not as well as age- and dosage-related differences in weight change.

RESULTS

Repeated-measures analysis of variance found no significant differences in weight change ($F = 0.66$, df = 1,120; $p = .80$) and no significant gender ($F = 0.65$, $p = .42$), dose ($F = 0.06$, $p = .81$), or age ($F = 0.08$, $p = .78$) effects nor difference between those who did and did not complete the trial ($F = 0.49$, $p = .48$) and no significant interaction of gender and completion status ($F = 0.33$, $p = .57$). Table 1 presents baseline and endpoint weights separately for the group of patients who dropped out or discontinued and for those patients who completed the 12 months of risperidone treatment; this comparison further illustrates that there was no significant weight change. Not one of the events leading to discontinuation was related to weight gain.

BMI at baseline was positively correlated with weight gain (for completers, N = 96, $r = 0.34$, $p = .001$). However, it should be noted that baseline BMI explains only 11% of the variance in weight observed in the present study.

DISCUSSION

In this 1-year open-label trial of risperidone among the elderly, we found no significant weight change. A recent meta-analysis by Allison et al.[4] that examined antipsychotic-induced weight gain among patients treated with conventional and atypical antipsychotics found that the weight gain after 10 weeks of risperidone treatment was 2.10 kg, which was less than that reported for clozapine, olanzapine, and sertindole and more than that reported for ziprasidone. However, as the authors themselves note, due to the limitations of information presented in each study, they were not able to examine the possible role of patients' characteristics such as age and sex.[4] The reasons why atypical neuroleptics are associated with weight gain are not clear. An interesting hypothesis is that the 5-HT_{2A} and 5-HT_{2C} receptors stimulate food intake and cause weight gain, and the atypical neuroleptics have high binding affinities for these receptor subtypes.[10] Similarly, it is not clear why elderly patients on treatment with neuroleptics did not gain weight in the present report.

In addition, Allison et al.[4] note their inability to estimate weight changes over an extended time of treatment. The current report presents data on weight change among the elderly in a 1-year open-label trial. Our findings demonstrate no weight gain in this group of patients. It should be noted that at endpoint, the mean risperidone dose for the group was 3.7 mg daily, which is within acceptable limits,[11] and so the findings cannot be attributed to a low treatment dose. The finding of the present study may be unique to elderly schizophrenia patients. Recently, Csernansky and Okamoto[12] have reported that in younger patients (mean ± SD age = 40.3 ± 10.4 years) treated with risperidone for a mean of 355 days, weight gain of 2.3 ± 0.64 kg (5.1 ± 1.4 lb) was recorded, which was statistically significant but only marginally clinically significant.

This study has several limitations. First, it had an open-label design; however, weight measurements are biological measurements not particularly influenced by the study design. Another limitation of the study is that the second weight measurement was missing for many of the patients who dropped out of the trial. It is thus possible that the persons who dropped out of the trial had more weight gain than those who remained in the trial. The study did, however, offer a high-powered test within the group who completed the trial. The 96 pairs of observations in this group affords 95% power to detect a weight change of at least 0.20 kg.

A further limitation is the participation of chronic schizophrenic patients who may have "attained" antipsychotic-induced weight gain during many years of previous exposure to typical antipsychotics.[13,14] Yet younger patients gain additional weight when switched to atypical drugs.[15] On the other hand, the long-term treat-

ment, large sample size, and homogenous inclusion criteria all suggest that our findings can be generalized to elderly patients suffering from chronic schizophrenia.

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

REFERENCES

1. Allison DB, Saunders SE. Obesity in North America: an overview. Med Clin North Am 2000;84:305–332
2. Himes CL. Obesity, disease, and functional limitation in later life. Demography 2000;37:73–82
3. Tsuang MT, Perkins K, Simpson JC. Physical diseases in schizophrenia and affective disorder. J Clin Psychiatry 1983;44:42–46
4. Allison DB, Fontaine KR, Heo M, et al. The distribution of body mass index among individuals with and without schizophrenia. J Clin Psychiatry 1999;60:215–220
5. Allison DB, Mentore JL, Heo M, et al. Antipsychotic-induced weight gain: a comprehensive research synthesis. Am J Psychiatry 1999;156: 1686–1696
6. Lacro JP, Eastham JH, Jeste DV, et al. Newer antipsychotics and antidepressants for elderly people. Curr Opin Psychiatry 1996;9:290–293
7. Madhusoodanan S, Brecher M, Brenner R, et al. Risperidone in the treatment of elderly patients with psychotic disorders. Am J Geriatr Psychiatry 1999;7:132–138
8. Kumar V, Brecher M. Psychopharmacology of atypical antipsychotics and clinical outcomes in elderly patients. J Clin Psychiatry 1999;60 (suppl 13):5–9
9. Davidson M, Harvey PD, Vervarcke J, et al. A long-term, multicenter, open-label study of risperidone in elderly patients with psychosis. Int J Geriatr Psychiatry 2000;15:506–514
10. Wirshing DA, Wirshing WC, Kysar L, et al. Novel antipsychotics: comparison of weight gain liabilities. J Clin Psychiatry 1999;60:358–363
11. Sajatovic M, Ramirez LF, Vernon L, et al. Outcome of risperidone therapy in elderly patients with chronic psychosis. Int J Psychiatry Med 1996;26: 309–317
12. Csernansky JG, Okamoto A. A long-term double-blind comparison of risperidone and haloperidol in stable outpatients with schizophrenia and schizoaffective disorder [abstract]. Int J Psychopharmacol 2000;3 (suppl 1):S155
13. Thomas PR, ed. Committee to Develop Criteria for Evaluating the Outcomes of Approaches to Prevent and Treat Obesity, Food and Nutrition Board, US Institute of Medicine. Weighing the Options: Criteria for Evaluating Weight Management Programs. Washington, DC: National Academy Press; 1995
14. Rothacker DQ, Blackburn GL. Obesity prevalence by age group and 5-year changes in adults residing in rural Wisconsin. J Am Diet Assoc 2000;100:784–790
15. Beasely CM Jr, Tollefson GD, Tran PV. Safety of olanzapine. J Clin Psychiatry 1997;58(suppl 10):13–17