Atypical Antipsychotics and Weight Gain in Chinese Patients: A Comparison of Olanzapine and Risperidone

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Objective: To compare the effect of olanzapine with that of risperidone on weight change among Chinese patients in Hong Kong.

Method: The body weight of subjects maintained on olanzapine or risperidone treatment was recorded at the outpatient clinic of a teaching hospital. Pretreatment weight of the subjects was retrieved from case records. Subjects on olanzapine treatment were matched in sex, age, and diagnosis with those on risperidone treatment, and demographic and clinical data were analyzed. The study was conducted in May and June 2002.

Results: Twenty-eight olanzapine-risperidone matched pairs were studied. All were diagnosed with DSM-IV schizophrenia. In patients treated with olanzapine and risperidone, respectively, mean ± SD duration of treatment with atypical neuroleptics was 103.5 ± 47.4 weeks and 93.2 ± 50.6 weeks (range, 21–255 weeks), and mean doses were 12.4 ± 6.7 mg/day and 4.5 ± 2.8 mg/day. The mean ± SD weight gain of subjects on treatment with olanzapine and risperidone, respectively, was 8.34 ± 5.97 kg (18.53 ± 13.27 lb) and 2.74 ± 8.09 kg (6.09 ± 17.98 lb) with a statistically significant difference at $p < .005$. Lower baseline body weight and body mass index were associated with greater weight gain in both olanzapine- and risperidone-treated subjects. Gender, age, mean daily dose, and duration of treatment had no effect on weight change.

Conclusion: Treatment with olanzapine was associated with significantly greater weight gain than treatment with risperidone in Chinese schizophrenia patients in Hong Kong. The effect of adjunctive anticonvulsant treatment on weight gain requires further study.

(J Clin Psychiatry 2004;65:864–866)

Received March 15, 2003; accepted Nov. 4, 2003. From the Department of Psychiatry, The Chinese University of Hong Kong, Hong Kong.

The authors report no financial affiliation or other relationship relevant to the subject matter of this article.

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Atypical antipsychotic drugs have been shown to have beneficial effects on positive, negative, and affective symptoms of schizophrenia. However, excessive weight gain remains a serious side effect. Reports suggest differences in weight change associated with different atypical antipsychotics.[1–4] Olanzapine is reported to induce more weight gain than risperidone.[5–7] However, the published data are from studies of subjects in Western countries, and as lipid metabolism, eating habits, and lifestyle differ between people of different ethnicities,[8,9] the problem of weight gain in Chinese subjects in Hong Kong remains undefined. The aim of this study was to determine the differences in weight change in local Chinese subjects treated with olanzapine or risperidone and explore the associated risk factors.

METHOD

The study was conducted in the outpatient department of Prince of Wales Hospital, a university teaching unit in Hong Kong, in May and June 2002. Patients receiving olanzapine or risperidone were weighed after giving informed consent when they attended follow-up in the study period. Pretreatment weight, clinical data, and demographic data were retrieved from the case records. Information on smoking habits and engagement in a weight reduction program was collected through phone contact. Patients with significant physical diseases, on a weight reduction program, or receiving anticonvulsants, antidepressants, lithium, or antipsychotics other than olanzapine or risperidone were excluded. Subjects on olanzapine treatment were matched in age, sex, and diagnosis with those on risperidone treatment. The data were analyzed with independent-sample t tests and bivariate correlation using the Statistical Package for the Social Sciences, version 10.0 (SPSS Inc., Chicago, Ill.).

RESULTS

A total of 179 Chinese subjects, 78 on olanzapine treatment and 101 on risperidone treatment, were recruited during the study period. After exclusion of patients with significant physical diseases, on a weight reduction program, or receiving the drugs listed in the exclusion crite-

ria, 34 subjects receiving only olanzapine and 49 subjects receiving only risperidone remained.

Of these 83 subjects, 28 olanzapine-risperidone pairs matched in age, sex, and diagnosis were obtained. Sixteen pairs were female and 12 pairs were male. All were diagnosed with DSM-IV schizophrenia. All subjects had undergone therapeutic trials of at least 2 typical antipsychotics before switching to olanzapine or risperidone. For olanzapine- and risperidone-treated subjects, respectively, mean ± SD age was 33.9 ± 12.0 years and 36.3 ± 10.0 years, mean duration of illness was 8.0 ± 6.1 years and 7.5 ± 5.3 years, mean duration of treatment with atypical neuroleptics was 103.5 ± 47.4 weeks and 93.2 ± 50.6 weeks (range, 21–255 weeks), mean dose was 12.4 ± 6.7 mg/day and 4.5 ± 2.8 mg/day (chlorpromazine equivalents, 496 ± 267 mg/day and 448 ± 279 mg/day), mean baseline body weight was 56.2 ± 8.3 kg (124.9 ± 18.4 lb) and 61.0 ± 10.4 kg (135.6 ± 23.1 lb), and mean baseline body mass index (BMI) was 21.0 ± 4.0 kg/m^2 and 22.6 ± 2.7 kg/m^2, with no significant statistical differences between the treatment groups. There was also no statistically significant difference in smoking habits between the 2 groups (32.1% [N = 9] of olanzapine-treated subjects smoked, 28.6% [N = 8] of risperidone-treated subjects smoked; $p > .05$).

Mean ± SD weight gain was 8.34 ± 5.97 kg (18.53 ± 13.27 lb) and 2.74 ± 8.09 kg (6.09 ± 17.98 lb) (15.50 ± 11.18% and 5.44 ± 13.97% of baseline body weight) for patients treated with olanzapine and risperidone, respectively, with a statistically significant difference ($p < .005$).

Mean weight gain was negatively associated with baseline body weight and pretreatment BMI (association with baseline body weight: $r = –0.42$, $p = .02$; association with pretreatment BMI: $r = –0.43$, $p = .02$, for both olanzapine and risperidone), while age, sex, mean daily dose, duration of illness, and duration of treatment had no effect on weight change.

DISCUSSION

Antipsychotics are associated with side effects that can jeopardize physical health and undermine treatment compliance.[10,11] Atypical antipsychotics were developed for better efficacy and less side effects. Both olanzapine and risperidone are recognized for their efficacy as antipsychotics, and their side effects have been widely studied.[12,13] Weight gain has been a focus of attention due to its adverse effect on various metabolic and physiologic functions,[14,15] as well as its social and personal impact. It defies the "keep-fit" subculture that has become the norm of young people today.[9] Most of our patients who suffer from psychosis and require antipsychotics belong to this age group.

Obesity is associated with physical predisposition and social origin. In addition to these factors, different neurotransmitters and blood leptin have been implicated in the differences in fat metabolism.[15–17] The phenomenon of weight gain in psychiatric patients is therefore likely to be multifactorial. So far, only studies in Western countries have been reported, but in view of cross-cultural diversities in eating habits and lipid metabolism,[8,9] local differences are to be expected.

In the current investigation, the mean weight gain with olanzapine treatment was 3 times as great as that with risperidone, 8.3 versus 2.7 kg (18.5 vs. 6.1 lb), over a period of 2 years. In contrast to the longer-term focus of this study, most studies have reported on short-term weight changes. Beasley et al.[18] and Nemeroff[19] observed mean weight increases of 3.5 kg in 6 weeks and 12 kg in 12 weeks, respectively, with olanzapine. Claus et al.[20] reported an average weight gain of 2 kg in 6 to 8 weeks with risperidone. A retrospective analysis suggests that weight gain associated with risperidone levels off after 12 weeks, while weight gain with olanzapine continues to increase over 20 weeks.[3] Our study supports the hypothesis that olanzapine induces not only greater but also more sustained weight gain than risperidone. Furthermore, when findings from different centers are compared,[3,5,6,20] weight gain among different ethnic groups with risperidone treatment remains relatively minor and stable, in the range of 2 to 3 kg, despite differences in genetic makeup and premorbid weight.

This study also highlights the negative association between weight gain and premorbid weight or BMI in both olanzapine and risperidone treatment. The finding seems universal and could be explained by lipid pathophysiology.[21] Chinese subjects have lower baseline body weight and BMI than white subjects.[22] The greater weight gain associated with olanzapine, both absolute and in percentage, could be associated with even greater physical and psychological morbidity in Chinese subjects. This hypothesis warrants further examination including direct comparison between different ethnic groups.

While most studies have reported that male subjects experience greater weight gain than female subjects, no significant gender difference was found in the current study. This contrast in findings could result from sample bias as there is male predominance in the Western samples.[22] Apart from sample bias, difference in pharmacologic properties among different ethnic groups could be an alternative explanation, and there are suggestions that nonwhite patients might experience greater weight gain.[23] The relatively longer duration of treatment in our subjects compared with those in other studies is another possible confounding factor.

The current study has several major limitations. The retrospective design, small sample size, retrieval of clinical data from case records, wide variation in duration of treatment, and lack of weight information in the early phases of treatment are major drawbacks. Only ob-

jective weight change was recorded, while other metabolic parameters and clients' perception of the phenomenon, including impact on treatment compliance, were not explored.[24] Moreover, because of the small sample size, the well-known synergistic effect of mood stabilizers, e.g., valproate, on weight gain could not be evaluated.

Despite various limitations, this study represents a preliminary effort to understand the relationship between weight gain and atypical antipsychotics in Chinese psychiatric patients in Hong Kong. Though providing little insight on short-term changes, the current investigation provides data on weight change with atypical antipsychotic treatment over an extended period of time. This information could be invaluable in the long-term management of patients suffering from psychotic illnesses. Prospective studies with larger sample sizes, biochemical evaluation of lipid metabolism, psychological appraisal of impact of weight gain, and assessment of the effect of adjunctive mood stabilizers on weight change are being planned so that better weight-control strategies can be devised.

Drug names: chlorpromazine (Thorazine, Sonazine, and others), lithium (Lithobid, Eskalith, and others), olanzapine (Zyprexa), risperidone (Risperdal).

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