Background: Olanzapine is temporally associated, in a number of patients with schizophrenia, with weight gain. H2 antagonists, like nizatidine, have been shown to control appetite in overweight patients.

Methods: A patient with olanzapine temporally associated weight gain was treated with nizatidine as “add-on” therapy.

Results: Nizatidine treatment was associated with good control and subsequent reduction of weight after 4 to 5 weeks of therapy in a patient with repetitive episodes of weight gain during olanzapine treatment. Olanzapine was otherwise well tolerated and effective in controlling psychopathology.

Conclusions: H2 antagonist treatment with olanzapine may be a valid medical strategy in preventing and/or reducing weight gain in patients with schizophrenia. Controlled studies are recommended to confirm this observation.

Key Words: Olanzapine, nizatidine, weight gain, schizophrenia, histamine

Introduction

It is well established that olanzapine is an effective and well-tolerated treatment of schizophrenia (Tollefson et al 1997); however, typical of many antipsychotics, olanzapine has been associated with weight gain (Wirshing et al 1999). The most significant predictors of olanzapine-associated weight gain, both statistically and in terms of magnitude of response, are an increased appetite, younger age, positive clinical response, and a low baseline body mass index (Kinon et al 1998). Dose is not a significant predictor of long-term changes in weight (Kinon et al 2000). The mechanism for olanzapine-related weight gain is unknown, although antagonism of serotonin and histamine receptors is hypothesized (Mercer et al 1994; Simansky 1996; Tecott et al 1995). We observed an unexpected weight loss in two schizophrenic patients on olanzapine who were concomitantly treated with nizatidine for peptic esophagitis. Indeed, published literature, preclinical and clinical, suggests that H2 receptor antagonists may induce weight loss in overweight conditions (Singh and Singh 1995; Stoa-Birketvedt 1993; Stoa-Birketvedt et al 1996, 1998) by suppression of gastric acid secretion (Stoa-Birketvedt 1992, 1993) or by a direct effect of histamine H2 blocking on appetite (Andersen et al 1992). Consequently, we decided to examine the effect of nizatidine added to olanzapine therapy in a patient with olanzapine-associated weight gain.

Case Study

A 23-year-old male patient with a DSM-IV diagnosis of paranoid schizophrenia received a 12-week treatment course of olanzapine (starting at the dose of 15 mg/day with an increase up to 20 mg/day) for his first episode of psychosis. His baseline weight was 78 kg and increased up to 82 kg after 4 weeks of treatment, with further increase to 86 kg (eighth week) and 90 kg (12th week). Despite a substantial amelioration of his psychopathology (Brief Psychiatric Rating Scale [BPRS] and Positive and Negative Syndrome Scale [PANSS] scores were reduced by 41% and 50%, respectively, from baseline to week 12), the patient decided to discontinue antipsychotic medication due to weight gain.

After 10 months of discontinuation, the patient’s weight returned to 76 kg, but he developed a relapse of psychotic symptoms. Olanzapine was therefore resumed at 10 mg/day and increased to 20 mg/day by day 8, and up to 25 mg/day by the sixth week. Once again, 4 weeks of treatment with olanzapine were associated with a 9% weight increase (from 76 kg to 82.5 kg) and a refusal to continue treatment, in spite of improved psychopathology; however, the patient was informed of the hypothesis that H2 antagonist adjunction might address the overweight phenomenon and gave his consent to receive nizatidine (150 mg b.i.d.) in conjunction with continued olanzapine treatment. After 4 weeks of concomitant therapy, his weight was substantially unchanged (83 kg); however, by the end of the eighth week of concomitant treatment his weight decreased by 5% to 79 kg (Figure 1), and his psychopathology remained improved (BPRS and PANSS.

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scores were reduced by 36% and 42% from baseline, respectively). The patient’s weight loss was maintained during 2 months of observation.

**Discussion**

The repetitive episodes of weight gain observed during the two periods of treatment with olanzapine suggest that weight gain was induced by the novel antipsychotic with a sufficiently predictable progression over time. The initial stabilization and the subsequent weight reduction during nizatidine adjunction were clinically remarkable. Although olanzapine plasma levels were not studied, the good therapeutic response to olanzapine administered with and without nizatidine is not consistent with the possibility that poor compliance and or pharmacokinetic changes may have produced the reversal of the olanzapine-induced weight gain phenomenon. On the other hand, changes in olanzapine absorption or transit in the gastrointestinal tract cannot be excluded. This encouraging case report seems to justify controlled clinical trials aimed to test the hypothesis that H₂ antagonism may represent a strategy for the control and/or prevention of olanzapine-induced weight gain.

**References**


