Weight gain management in patients with schizophrenia during treatment with olanzapine in association with nizatidine

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Abstract

Objective: Weight gain is associated with treatment with many psychotropic agents. Nizatidine, H2 receptor antagonist, has been proposed to have weight-reducing effects. This was a 12-week, randomized, double-blind, placebo-controlled trial to evaluate the efficacy of nizatidine in reducing/restricting weight gain in patients with schizophrenia who have been under treatment with olanzapine. Method: Patients receiving olanzapine (2 to 6 months) and weight gain ≥5% of their body weight during olanzapine treatment were randomly assigned to receive nizatidine 600 mg or placebo for up to 12 weeks. Change in psychopathology was assessed using Brief Psychiatric Rating Scale scores from baseline to endpoint. Safety was assessed using the Safety Assessed Software, assessment of glucose and lipid blood levels, and treatment-emergent adverse events. Results: Out of 54 patients enrolled in this analysis, 45 completed the protocol. The mean weight change prior randomization was 7.6 kg and 7.3 kg for those randomized to placebo and nizatidine, respectively (p = 0.828). Patients receiving placebo and nizatidine had a mean weight gain of 12.3% (0.7 kg) and 12% (1.1 kg) from baseline to endpoint, respectively (p = 0.9). Patients from both groups experienced a statistically significant decrease on the Brief Psychiatric Rating Scale mean score from baseline to endpoint. Treatment-emergent adverse events were reported by 18.5% and 25.9% on the placebo and nizatidine group, respectively. There were no statistically significant differences in glucose and lipid blood levels from baseline to endpoint and between groups. Conclusions: The concomitant use of olanzapine with nizatidine was not effective in controlling weight gain in patients who had previously gained weight during treatment with olanzapine when compared to placebo.

Descriptors: Schizophrenia; Antipsychotics agents; Weight gain; Clozapine; Nizatidine

Resumo

Objetivo: Ganho de peso está associado ao tratamento com inúmeros psicotrópicos. O uso de nizatidina, um antagonista H2, pode estar associado à redução de peso. Este foi um ensaio clínico aleatorizado, duplo-cego, controlado com placebo, de 12 semanas, desenhado para avaliar a eficácia da nizatidina em reduzir/limitar o ganho de peso em pacientes com esquizofrenia recebendo olanzapina. Método: Pacientes recebendo olanzapina (dois a seis meses) com ganho de peso ≥ 5% do início do tratamento foram aleatorizados para receber nizatidina 600 mg ou placebo. Alterações psicopatológicas foram avaliadas usando-se a Escala de Avaliação Psiquiátrica Breve no final do estudo. Segurança foi avaliada por meio da pontuação no Safety Assessed Software, avaliação dos níveis de glicemia e lipídios e a incidência de eventos adversos decorrentes do tratamento. Resultados: Dos 54 pacientes incluídos na análise, 45 completaram o protocolo. A alteração média de peso antes da aleatorização foi de 7,6 kg e 7,3 kg nos pacientes aleatorizados para placebo e nizatidina, respectivamente (p = 0,828). Pacientes recebendo placebo e nizatidina tiveram, respectivamente, ganho médio de peso de 12,3% (7 kg) e 12% (1,1 kg) ao longo do estudo (p = 0,9). Ambos os grupos apresentaram diminuição estatisticamente significativa na pontuação média da Escala de Avaliação Psiquiátrica Breve. Eventos adversos emergentes do tratamento foram relatados por 18,5% e 25,9% dos pacientes recebendo placebo e nizatidina, respectivamente. Não houve diferença estatisticamente significativa nos níveis glicêmicos e lipídicos do início ao final do estudo e entre os grupos de tratamento. Conclusões: Comparado ao placebo, o uso concomitante de olanzapina e nizatidina não foi eficaz em controlar o peso em pacientes com ganho prévio de peso durante o tratamento com olanzapina.

Descritores: Esquizofrenia; Agentes antipsicóticos; Ganho de peso; Clozapina; Nizatidina

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Financing: This clinical trial was sponsored by Eli Lilly do Brasil Ltda

Mauricio Silva de Lima and Oswaldo Bracco are Lilly employees.

Submitted: September 5, 2005
Accepted: July 21, 2006

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Introduction

According to the mental health supplement of the National Health Interview Survey, body mass index (BMI) distribution of schizophrenic individuals is generally similar to or higher than that of the general population, and weight changes in schizophrenic patients were well documented even in the pre-antipsychotic drug era. The reported prevalence of overweight and obesity in patients with schizophrenia has been found to range from 40% to 62%, and obesity is a complicating factor in many medical illnesses commonly seen in patients with schizophrenia. Atypical antipsychotics are associated with superior tolerability, compliance, and relapse prevention and have led to improved treatment for patients with serious mental illness. However, novel antipsychotics apparently produce an even greater weight gain when compared to typical agents. A recent meta-analysis of over 80 studies on weight change during antipsychotic treatment showed a mean weight gain after 10 weeks of treatment of 9.8 lb (4.45 kg) with clozapine, 9.1 lb (4.15 kg) with olanzapine, and 4.6 lb (2.10 kg) with risperidone compared to 2.4 lb (1.08 kg) with the typical antipsychotic haloperidol. Many theories (including increased food intake) have been advanced to explain the antipsychotic-related weight gain in schizophrenia. Recently, serotonin, dopamine, and histamine receptor blockade has been implicated.

In this manuscript, it is of particular interest the role of histamine in the regulation of appetite and satiety as it is well known that atypical antipsychotics have a much greater affinity to the H-1 receptor when compared to typical medications. This fact is consistent with the hypothesis that effects on histamine may contribute to atypical antipsychotic-treatment associated weight gain. Cimetidine, an H-2 receptor antagonist, has been reported to reduce weight in overweight healthy subjects, and also in overweight type 2 diabetes mellitus patients, although this finding has not been unequivocal. Gastrointestinal regulatory peptides, such as cholecystokinin, have been proposed to mediate the satiety signal from gut to brain. In normal subjects, cimetidine increased the basal cholecystokinin and may be one mechanism by which it reduces the appetite. A report by Sacchetti et al. described a patient with repeated episodes of weight gain during olanzapine treatment who experienced weight reduction after 4 to 5 weeks of therapy with nizatidine (150 mg BID), an H-2 antagonist. In a 16-week double-blind trial, Cavazoni et al. reported significantly less weight gain at weeks 3 and 4 with olanzapine+nizatidine 300 mg BID compared to olanzapine+placebo, although no statistical difference between groups was seen at 16 weeks. In that study, nizatidine was well-tolerated and did not adversely affect clinical outcomes. In an open-label study, Lopez-Mato et al. described that ranitidine also prevented or corrected weight gain in patients receiving olanzapine. The studies by Cavazoni et al. and Lopez-Mato et al. showed that H2 antagonists may prevent or reduce weight gain when initiated concomitantly with olanzapine treatment. During the treatment with olanzapine, approximately 25% of schizophrenic patients have a decrease in body weight or gain no weight. In those individuals, a pharmacological approach to control weight gain is certainly not recommended. According to a review by Kinon et al., approximately 48% of olanzapine-treated patients gain less than 7%. For these patients, behavioral and dietary changes may suffice to manage their body weight changes and no pharmacological approaches would be necessary.

The purpose of the present study was to evaluate whether the use of an H2 antagonist in schizophrenic patients who have already gained weight could promote stabilization or reduction in body weight. Additionally, patients were considered responders if remained in therapy for 6 weeks or more and had no weight gain or a weight gain ≤ 3% since started using nizatidine (baseline). Non-responders were defined as any patients who failed to remain at least 6 weeks in the study and had gained > 3% since starting treatment with nizatidine. Possible effects of nizatidine on psychopathology and safety parameters were also assessed.

Method

1. Sample

Outpatient subjects (male or female, 18 to 65 years of age) met DSM-IV diagnostic criteria for schizophrenia, schizoaffective disorder, or schizophreniform disorder. After a complete description of the study to the subjects, written informed consent was obtained. In order to be eligible to participate in this protocol, patients had to be in treatment with olanzapine (5 to 20 mg/day) for no less than 2 months and no more than 6 months, had a record of their body weight when initiated on olanzapine, had gained ≥ 5% since initiated the treatment with olanzapine, and had a total BPRS score < 45. Patients were excluded if they had any known physical illness that could affect body weight and composition, were currently participating in a formal weight loss program, or had a body mass index (BMI) ≥ 40 kg/m² or weight ≥ 114 kg. Patients with a diagnosis of diabetes mellitus could be enrolled provided their condition was under control and if they were in treatment for DM for at least 6 months. The study protocol was approved by Hospital Mario Kroeff Ethical Review Board on the 28th November 2002.

2. Study design

This was a randomized, double-blind, 12-week placebo-controlled trial. After a complete description of the study to the subjects, written informed consent was obtained. After baseline assessments, all eligible patients were randomized to receive placebo (PBO) or 300 mg nizatidine BID (NIZ). This study had a total of 4 follow-up interviews and assessments were performed in a monthly basis. Figure 1 shows the study design.

3. Assessments

Patients were weighed at each visit. All investigators were given detailed instruction at study start-up on uniform and consistent weight measurements. Psychopathology was assessed using the total score of the 18-item Brief Psychiatric Rating Scale (BPRS; each item rated from 1 to 7). Safety parameters were assessed by treatment-emergent adverse events, routine laboratory analytes, and extrapyramidal symptoms (EPS), measured by the total score of the Simpson–Angus Scale. Treatment-emergent adverse events were considered those that worsened or were described for the first time after initiating the treatment with nizatidine.

4. Statistical analysis

A mixed-effects model for repeated measures analysis of variance (ANOVA) was used to analyze the primary outcome measure (i.e. mean changes in total body weight from baseline to endpoint) and other continuous data. When the distribution was not normal, it was used the Mann-Whitney non-parametric test. For the comparison between responders and non-
randomized. There was no statistical difference in the mean percentage of weight gain before randomization to PBO or NIZ (PBO = 12.3%, NIZ = 12%) (p = 0.829). Table 2 shows body weight mean values before and during the study. The mean duration on olanzapine treatment, before being randomized to nizatidine or placebo, was 2.9 months for both groups. Among the 54 patients included in the analysis, none had a previous diagnosis of diabetes and none developed DM during the 12-week period of the study.

There were no statistical or clinical significant differences between genders. From the baseline assessment females had a 12.5% increase in body weight after the beginning of olanzapine treatment and males 11.9%, with BMC of 26.0 and 26.3 for females and males, respectively.

Table 1 - Sociodemographic and clinical characteristics at baseline for both treatment groups

<table>
<thead>
<tr>
<th></th>
<th>Placebo</th>
<th>Nizatidine</th>
<th>Total</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age (SD) – years</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gender (%/n)</td>
<td>Female</td>
<td>13 (48.1%)</td>
<td>22 (40.7%)</td>
<td>0.27</td>
</tr>
<tr>
<td></td>
<td>Male</td>
<td>14 (51.9%)</td>
<td>32 (59.3%)</td>
<td></td>
</tr>
<tr>
<td>Ethnicity (%/n)</td>
<td>White</td>
<td>16 (59.3%)</td>
<td>36 (66.7%)</td>
<td>0.45</td>
</tr>
<tr>
<td></td>
<td>Black/ mulatto</td>
<td>9 (33.3%)</td>
<td>14 (25.9%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Other</td>
<td>2 (7.4%)</td>
<td>4 (7.4%)</td>
<td></td>
</tr>
<tr>
<td>Body weight when initiating treatment with olanzapine (kg; SD)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>64.3 (12.2)</td>
<td>64.8 kg (13.4)</td>
<td>64.5 (12.7)</td>
<td>0.76</td>
</tr>
<tr>
<td>Mean time between time initiating on OLZ and baseline (months)</td>
<td>2.9 (1.1)</td>
<td>2.9 (1.2)</td>
<td>2.9 (1.1)</td>
<td>0.87</td>
</tr>
<tr>
<td>Age at first episode (years; SD)</td>
<td>24.9 (8.4)</td>
<td>22.3 (6.4)</td>
<td>23.6 (7.5)</td>
<td>0.21</td>
</tr>
<tr>
<td>Mean number of previous episodes (SD)</td>
<td>4.7 (5.0)</td>
<td>3.2 (4.3)</td>
<td>4.0 (4.7)</td>
<td>0.12</td>
</tr>
<tr>
<td>Hospitalization during the last 6 months</td>
<td>Yes</td>
<td>15 (55.6%)</td>
<td>24 (44.4%)</td>
<td>0.23</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>12 (44.4%)</td>
<td>30 (55.6%)</td>
<td></td>
</tr>
</tbody>
</table>

Results

1. Sociodemographic and clinical characteristics

A total of 54 patients were included in this analysis; 27 patients were randomized to receive nizatidine 300 mg BID and 27 to receive placebo, in association with their usual treatment with olanzapine (5-20 mg/day). Forty-five patients completed the treatment with no statistical difference between completers in both groups (p = 0.39). Age at first episode, number of previous episodes and hospitalizations during the last 6 months were assessed and groups were comparable regarding those clinical characteristics at baseline (Table 1). Additionally, the groups did not differ in terms of sociodemographic characteristics (Table 1). Out of the total sample, 59.3% (n = 32) were male and the mean age was 35.2 (SD ± 12.2).

Patients had to have an increase of at least 5% in their body weight from the time they initiated on olanzapine and were randomized. There was no statistical difference in the mean percentage of weight gain before randomization to PBO or NIZ (PBO = 12.3%, NIZ = 12%) (p = 0.829). Table 2 shows body weight mean values before and during the study. The mean duration on olanzapine treatment, before being randomized to nizatidine or placebo, was 2.9 months for both groups. Among the 54 patients included in the analysis, none had a previous diagnosis of diabetes and none developed DM during the 12-week period of the study.

There were no statistical or clinical significant differences between genders. From the baseline assessment females had a 12.5% increase in body weight after the beginning of olanzapine treatment and males 11.9%, with BMC of 26.0 and 26.3 for females and males, respectively.

2. Effect on weight

Both groups did not significantly differ with respect to amount of weight gain at endpoint: patients receiving NIZ had a mean weight gain of 1.1 kg and those randomized to PBO gained 0.7 kg (p = 0.9). Figure 2 shows the change in body weight between groups. Multiples comparisons along treatment visits,
regardless of treatment groups, showed that body weight at endpoint was statistically, although not clinically (< 5%), higher when compared to baseline (V1 versus V4: \( p = 0.002 \)); however, body weight at endpoint was significantly lower when compared to those at Visits 2 and 3 (V2 versus V4: \( p = 0.003 \), and V3 versus V4: \( p = 0.001 \)).

### 3. Responders and non-responders

53.8% \((n = 28)\) were considered responders, i.e., remained in therapy for at least 6 weeks and had no weight gain or had weight gain \(\leq 3\%\) since started using nizatidine (baseline). There was no statistical difference in the rates of responders for nizatidine 57.7% and placebo 50% \((p = 0.58)\). Females had a lower responder rate (39.3%), when compared to males (60.7%), but this difference was not statistically significant \((p = 0.63)\).

### 4. Effect on psychopathology and safety

Significant improvement on the BPRS total scores was observed in both treatment groups from baseline to endpoint \((p < 0.001 \text{ for both groups})\). However, the BPRS score was not significantly different between groups at endpoint \((\text{PBO: } 23.7 \pm 9.9; \text{NIZ: } 24.2 \pm 8.5; p = 0.12)\). Figure 3 shows the changes in BPRS total score from baseline to endpoint in both groups. Decreases in BPRS total score were seen as early as week 4 \((\text{V1 - NIZ: } 27.5; \text{PBO: } 23.9 \text{ vs. V2 - NIZ: } 25.4; \text{PBO: } 21.8; p = 0.006)\).

All patients showed a statistically significant improvement on the Simpson–Angus Scale from baseline to endpoint \((p < 0.001)\). There were no statistically significant differences between groups at endpoint \((\text{PBO: } 1.4 \pm 2.8; \text{NIZ: } 0.6 \pm 1.3; p = 0.51)\). There were no significant differences in treatment-emergent adverse events reported between groups \((\text{NIZ: } 25.9\% \text{ versus PBO: } 18.5\%; p = 0.5)\), and only 3 patients \((1 \text{ NIZ; 2 PBO})\) discontinued the study due to an adverse event. Headache, somnolence, and hypersomnia were the only treatment-emergent adverse events reported by more than 2 patients. There were no significant differences between groups on any of the measured laboratory analyses (Table 3).

### Discussion

The appropriate selection of APs ought to be based on drug efficacy and risk factors in clinical daily practice. Although more efficacious in a number of clinical outcomes, treatment with atypical antipsychotics may be associated with weight gain.\(^{11-13}\) Thus, patients should be informed of that adverse event in order to avoid excessive weight gain. Nutritional advice must be given and regular physical exercise recommended. Many studies have shown that behavioral, pharmacological or a combination of both methods turned out to be efficacious in preventing weight gain.\(^{13,26,32}\)

At present, there is no standardized pharmacological treatment for antipsychotic-related body weight gain. Some studies have assessed the effects of agents such as amantadine, orlistat,
metformin, nizatidine, and topiramate as pharmacological alternatives to manage this adverse event.26,33-37 Treating weight gain with pharmacological agents in psychiatric patients must be done with caution as some drugs used to this purpose may exacerbate the psychiatric condition, once their primary site of action is the central nervous system.12 Thus, the use of a medication to manage weight gain in psychiatric patients without central activity would be of particular interest.12

Previous studies showed that H2 antagonists might be related to weight loss in humans.21-22,25-27 Causing weight loss by a mechanism that is yet to be defined, H2 antagonists are more likely to have their the primary site of action outside the central nervous system, as H-2 antagonists as a class are very hydrophilic and cross the blood–brain barrier to a limited extent.38 Due to their peripheral site of action, H2 antagonists were used in some studies to manage weight gain in schizophrenic patients on olanzapine. Among those studies two are of most interest due to their design and methodology.26-27

Cavazzoni et al. compared two different doses of nizatidine (300 mg QD and 300 mg BID) with placebo to manage weight gain in patients initiating treatment with olanzapine.26 At weeks 3 and 4, patients treated with nizatidine 300 mg BID reported significantly less weight gain compared to placebo; however, no significant difference between the treatment groups was seen at 16 weeks. The authors suggested that nizatidine 300 mg BID may have a potential effect, albeit transient and possibly dose-related. The authors hypothesized a rebound phenomenon of weight recovery, a decrease in compliance over time, and interindividual variability as possible reasons for the apparent lack of persistent effect of nizatidine in controlling weight gain.

Lopez-Mato et al. evaluated the efficacy of different doses of ranitidine in preventing or reducing weight gain in schizophrenic patients treated with olanzapine in an open-label trial.27 According to their results, the use of ranitidine prevented or corrected weight gain in 59.6% of the patients receiving olanzapine. Patients not receiving ranitidine exhibited an average weight gain of 3.4 kilograms (SD: -2.5 to +16 kg), and an increase of 1.19 kg/m² in their BMI. Patients treated with ranitidine 300 mg/day gained 0.9 kilogram (SD: -4 and +10.6 kg), with an increase of 0.34 kg/m² in their BMI. For patients on the highest dose of ranitidine (600 mg), the weight gain curve trended towards normalization. They lost 1.6 kilogram and 0.6 points in their BMI, in average. Additionally, they lost up to –15 kilograms and gained less weight (up to 7 kilograms) when compared to those receiving a lower dose of ranitidine or placebo. Contrary to the study of nizatidine by Cavazzoni et al. the effect of weight control with ranitidine was sustained along all the study period.26

Table 3 - Laboratory analytes between treatment groups and from baseline to endpoint

<table>
<thead>
<tr>
<th></th>
<th>V1 (week 0)</th>
<th>V4 (week 12)</th>
<th>p-value NIZ vs. PBO</th>
<th>p-value V1 vs. V4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glicemia</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PBO</td>
<td>83.3 (10.2)</td>
<td>84.6 (14.7)</td>
<td>0.414</td>
<td>0.006</td>
</tr>
<tr>
<td>NIZ</td>
<td>85.4 (12.0)</td>
<td>87.1 (14.5)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cholesterol total</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PBO</td>
<td>191.3 (36.8)</td>
<td>180.3 (34.1)</td>
<td>0.241</td>
<td>0.830</td>
</tr>
<tr>
<td>NIZ</td>
<td>195.6 (47.0)</td>
<td>198.8 (46.0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HDL</td>
<td>49.2 (9.4)</td>
<td>46.5 (12.7)</td>
<td>0.8</td>
<td>0.9</td>
</tr>
<tr>
<td>NIZ</td>
<td>48.7 (13.4)</td>
<td>45.8 (10.6)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>LDL</td>
<td>191.3 (36.8)</td>
<td>180.3 (34.1)</td>
<td>0.34</td>
<td>0.77</td>
</tr>
<tr>
<td>PBO</td>
<td>186.5 (47.0)</td>
<td>198.8 (46.0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Triglycerides</td>
<td></td>
<td></td>
<td>0.38</td>
<td>0.28</td>
</tr>
<tr>
<td>PBO</td>
<td>146.2 (71.0)</td>
<td>152.7 (75.1)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NIZ</td>
<td>168.4 (120.0)</td>
<td>178.4 (112.7)</td>
<td></td>
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</tr>
</tbody>
</table>

Figure 3 - Changes in BPRS total score from baseline to endpoint according to treatment groups
Our study had the main objective of assessing whether an H2 antagonist, nizatidine, could be of help for patients with schizophrenia or related disorders that had already had substantial weight gain (≥ 5%) with olanzapine. If so, it would avoid unnecessary use of this pharmacological strategy to a significant part of patients who, during the course of their treatment with olanzapine, did not present weight gain nor had a weight gain that could be managed by behavioral and/or dietary strategies.  

We demonstrated that nizatidine when administered to olanzapine-treated patients with previous weight gain did not differ from placebo in the amount of weight control. It could be hypothesized that the greater increases in body weight occurred most likely during the first months after initiating treatment with olanzapine (pre-study). Patients randomized to nizatidine gained on average 6.8 kg and those randomized to placebo, 6.5 kg, during that study period. Although continuing gaining weight, this increase was substantially lower (NIZ: 1.1kg and PBO: 0.7 kg) when compared to the initial phase of treatment with olanzapine. Those results are in accordance with previously published data, showing that the rate of weight gain appears to be more intense during the first 12 weeks of olanzapine treatment, occurring less rapidly in subsequent weeks, and plateauing around the 39th week. That might be one explanation why nizatidine did not differ from placebo in controlling weight as most patients could already be in or close to the plateau phase.  

Another concern related to the use of atypical antipsychotics is the potentially increased risk of treatment-emergent diabetes. Contrary to weight gain, that has been reported with some atypicals more than others (e.g., clozapine, olanzapine), recent reviews show that the potentially increased risk of DM appears to be a class-wide occurrence among the new generation antipsychotics. In our study, blood glucose and lipids levels did not differ from baseline to endpoint and between patients in the two treatment groups during the 12 weeks of the study duration.  

There are consistent data suggesting that the main driver when choosing an antipsychotic treatment must be the drug efficacy. Although treated as a homogeneous group, effectiveness is different from one drug to another. For instance, in a recent meta-analysis, Davis et al. described that only clozapine, amisulpride, risperidone, and olanzapine were more efficacious than typicals, while other atypicals were not. After considering the drug's efficacy, medication's risk profile must also be considered.  

According to measures in the levels of psychopathology, extrapyramidal symptoms, laboratory analyzes, and reports of treatment-emergent adverse events assessed during the study, nizatidine did not interfere with the efficacy and/or safety of olanzapine. This study did not have the intention to determine the efficacy or safety of olanzapine. Patients’ levels of psychopathology were followed-up in the trial by using BPRS. Patients included in this study were not in an acute phase during the first weeks of treatment, results might have favored this intervention.  

Finally, only body weight at the time olanzapine was initiated was a required measure to be enrolled in this study, yet no requirement was made regarding metabolic parameters. Any conclusion about changes in those analyses must be taken very cautiously. The same caution must be observed regarding conclusions on psychopathology and extrapyramidal symptoms, as the study was not designed for purposes of efficacy and/or safety.  

Conclusions  
Our results showed that, when patients had already gained substantial weight with olanzapine treatment, the concomitant use of nizatidine did not differ from placebo in controlling weight gain. Olanzapine shows a remarkable efficacy in improving psychopathology in schizophrenic patients; however, some patients may experience significant weight gain. Innumerable studies show that weight gain can be adequately and successfully managed with behavioral and/or pharmacological approaches. The relatively rapid onset of weight gain with olanzapine suggests the importance of early intervention for weight gain mitigation. Proactive interventions to deal with this adverse event, regardless of the nature of the intervention, may result in weight stabilization/loss. Furthermore, appropriate attention to this issue can improve the quality of life for patients treated with antipsychotic drugs, and decrease morbidity and mortality due to weight-related disorders.

References


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