Olanzapine Treatment of Anorexia Nervosa: A Retrospective Study

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Abstract: Background: Recent reports raise the possibility that olanzapine, which commonly causes weight gain in non–eating-disordered subjects, assisted weight gain and mood during refeeding in anorexia nervosa (AN) patients. Methods: Eighteen AN subjects who engaged in open treatment with olanzapine were retrospectively questioned about their response. Results: Subjects reported a significant reduction in anxiety, difficulty eating, and core eating disorder symptoms after taking olanzapine. Discussion: These data lend support to the possibility that olanzapine may be useful in AN patients. Conclusion: A controlled trial is necessary to prove that olanzapine is efficacious. © 2003 by Wiley Periodicals, Inc. Int J Eat Disord 33: 234–237, 2003.

Key words: olanzapine; weight gain; anorexia nervosa; psychiatric disorder

INTRODUCTION

Anorexia nervosa (AN) is a disorder of unknown etiology that predominantly occurs in women (American Psychiatric Association, 1994). It is characterized by restricted eating, the relentless pursuit of thinness, and obsessive fears of being fat. These symptoms result in profound weight loss and considerable psychological morbidity. Because of limited efficacy of existing treatments, many people with AN often have a chronic, recurring illness (Herzog, Nussbaum, & Marmor, 1996). Moreover, AN has the highest death rate of any psychiatric disorder (Sullivan, 1995). The hospital utilization rate for people with AN is higher than for any other psychiatric disorder, aside from schizophrenia and organic mental disorders (McKenzie & Joyce, 1992). Extended hospitalizations, which can restore weight to emaciated individuals, can be life-saving and can reverse medical complications, but are lengthy and expensive (Anderson, Morse, & Santmyer, 1985).

Short-term weight restoration has had limited effect on future outcome. The Maudsley study (Russell, Szmukler, Dare, & Eisler, 1987) reported that only 23% of the patients had...
a good outcome 1 year after being hospitalized for weight restoration. This is because pharmacologic and psychological treatments for AN patients have been of limited efficacy. For example, pharmacologic treatments (antidepressants including selective serotonin reuptake inhibitors [SSRIs] and neuroleptics) that have focused on increasing weight and reducing symptoms in emaciated patients have had little success (Hoffman & Halmi, 1993). Kaye et al. (2001) found that fluoxetine, in a controlled trial, prevented recurrence and reduced obsessionality and depression when administered after weight restoration in women with AN. However, recent limitations of health care coverage have resulted in shorter lengths of inpatient treatment for patients with AN (Silber, 1994). As a result, anorexics are often discharged while still being underweight.

Administration of the atypical neuroleptics is often associated with weight gain as a side effect. Weight gain is most significant with clozapine, but it is also well documented with risperidone, sertrindole, and olanzapine. Patients in studies with risperidone, sertrindole, and olanzapine have gained, on average, approximately 2–8 lb (1–4 kg) over the first 6–8 weeks of study. Longer-term treatment studies have shown that some patients continue to gain several more pounds (kilograms) before their weight stabilizes (Casey, 1996; Gupta, Droney, Al-Samarrai, Keller, & Frank, 1999). Of the atypical neuroleptic agents, olanzapine has the most favorable side effect profile (Reus, 1997). In addition, these drugs may be useful in reducing severe agitation and mood lability. These properties led to an open-label trial of olanzapine among several particularly agitated and resistant, underweight AN patients. Several case reports have suggested that olanzapine may be helpful in increasing weight and improving mood in underweight AN patients (Hansen 1999; Jensen & Mejhlhed, 2000; La Via, Gray, & Kaye, 2000; Mehler et al., 2001, Powers, Santana, & Bannon, in press).

**METHOD**

Conventional assessments of depression and anxiety did not accurately assess the unique characteristics of AN patients or the effects of olanzapine on core eating disorder behaviors. We devised a 10-question, 5-point anchored scale of AN-related behaviors that were potentially improved by olanzapine (Table 1).

We contacted 30 AN subjects who received olanzapine while in the inpatient eating disorders program and asked them to complete a questionnaire assessing their recollection

Table 1. Retrospective self-report of estimation of symptoms before and during olanzapine treatment.

<table>
<thead>
<tr>
<th>Scale</th>
<th>Entry Score $(M \pm SD)$</th>
<th>At Time of Contact $(M \pm SD)$</th>
<th>$t$</th>
<th>$p$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Obsessive thoughts about body image</td>
<td>4.6 ± 0.7</td>
<td>3.4 ± 1.1</td>
<td>5.4</td>
<td>.000</td>
</tr>
<tr>
<td>Appetite (thoughts about hunger)</td>
<td>2.1 ± 1.1</td>
<td>2.4 ± 1.1</td>
<td>–1.1</td>
<td>.27</td>
</tr>
<tr>
<td>Anxiety before and during meals</td>
<td>4.3 ± 0.9</td>
<td>3.2 ± 1.0</td>
<td>5.0</td>
<td>.000</td>
</tr>
<tr>
<td>Ability or desire to eat meals</td>
<td>4.4 ± 0.9</td>
<td>2.7 ± 1.2</td>
<td>6.8</td>
<td>.000</td>
</tr>
<tr>
<td>General anxiety (in social situations, worrying about what might happen)</td>
<td>3.8 ± 1.2</td>
<td>3.1 ± 1.2</td>
<td>4.1</td>
<td>.001</td>
</tr>
<tr>
<td>Daytime sleepiness</td>
<td>2.1 ± 1.2</td>
<td>2.6 ± 1.2</td>
<td>–1.5</td>
<td>.16</td>
</tr>
<tr>
<td>Nighttime ability to fall asleep</td>
<td>4.1 ± 1.1</td>
<td>1.9 ± 1.3</td>
<td>7.4</td>
<td>.000</td>
</tr>
<tr>
<td>Reactivity to stress, mood stability</td>
<td>3.8 ± 1.3</td>
<td>2.9 ± 1.1</td>
<td>2.9</td>
<td>.01</td>
</tr>
<tr>
<td>Reaction to weight gain, mood increase</td>
<td>4.2 ± 1.0</td>
<td>3.4 ± 1.3</td>
<td>3.8</td>
<td>.002</td>
</tr>
<tr>
<td>Dizziness immediately after standing</td>
<td>2.7 ± 1.7</td>
<td>1.8 ± 1.0</td>
<td>2.5</td>
<td>.02</td>
</tr>
</tbody>
</table>

Note: The higher the score, the more severe the symptoms.
of their behaviors before and after administration of olanzapine. The subjects were initially contacted through a letter sent by the clinical staff informing them of the study. After giving informed consent, the subjects were contacted for the follow-up interview either over the phone or in person, at which time a clinical research nurse or medical student administered the questionnaire. Subjects were asked to answer each question twice, once for how they felt during their illness before receiving olanzapine (entry score) and a second time for how they felt when they received olanzapine (exit score). Five of the subjects had also received SSRIs, 2 had been using benzodiazepines, and 3 had received both medications.

RESULTS

Eighteen AN subjects agreed to complete this retrospective questionnaire in person or via a phone interview. They were 22 $\pm$ 7 years old (range, 16–37 years old) and had developed AN when they were 16 $\pm$ 5 years old. Before starting olanzapine, they weighed 38 $\pm$ 6 kg. When questioned, they weighed 43 $\pm$ 6 kg. They took 4.7 $\pm$ 2.4 mg of olanzapine a day (range, 2.5–10 mg) and had been on olanzapine for 17 $\pm$ 20 weeks (range, 3–70 weeks).

Subjects reported a significant reduction ($p < .001$) in frequency of obsessive thoughts about body image and fear of being fat (Table 1). Subjects said they had reduced anxiety ($p < .001$) before and during meals and an increased ability or desire ($p < .001$) to eat their meals. In addition, subjects reported being less upset if they gained weight ($p = .002$). Subjects also reported being significantly ($p < .01$) less reactive or upset in response to stress or social situations and slept better at night.

There were no relationships between age, duration of illness, body weight at entry or exit, or medication status and response to treatment.

DISCUSSION

These retrospective data provide further support that olanzapine may be useful in reducing core symptoms and in restoring weight in AN patients (Hansen, 1999; Jensen & Mejlhede, 2000; La Via et al., 2000; Powers et al., in press).

Because olanzapine interacts with dopaminergic, serotonergic, adrenergic, and muscarinic receptors (Bymaster et al., 1997), the neuronal systems responsible for this drugs’ potential efficacy remain uncertain. Considerable animal and human studies implicate serotonin activity in feeding (Leibowitz, 1990), obsessionality (Barr, Goodman, Price, McDougle, & Charney, 1992), and anxiety (Charney, Woods, Krystal, & Heninger, 1990), which are altered in AN patients. Recent physiologic data from positron emission tomography (PET) imaging and biological studies (Frank et al., 2002; Kaye et al., 2002) support the speculation that subjects with AN have disturbances of serotonin activity, which opens the possibility of understanding how olanzapine may be beneficial in the treatment of AN.

This investigation relied on a retrospective strategy with a newly designed and non-standardized assessment instrument. There is no comparison group and the perceived effects of olanzapine may have been confounded by the cumulative effects of the multi-disciplinary treatment program. Because not all subjects who took olanzapine cooperated with this study, it is possible that an assessment bias contributed to the robustness of these findings. These data must be considered with extreme caution. However, it is well accepted that people with AN are often resistant to treatment and taking medication. It is
noteworthy that many subjects cooperated with this study and were compliant with olanzapine administration. A controlled trial will be necessary to demonstrate whether olanzapine, or any of these class of drugs, is an effective clinical treatment for AN patients.

In summary, based on the initial clinical improvements and the few side effects (mild sedation), olanzapine may be a promising agent for people with AN. This medication, and possibly other similar drugs, offers the possibility of a much-needed addition to the treatment regimen for AN patients. Currently, there are no effective pharmacotherapies that significantly improve behavior in anorectic patients, a population that represents high morbidity/mortality rates and incurs substantial health care costs.

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REFERENCES


