CASE REPORT

Use of Mirtazapine in an Adult with Refractory Anorexia Nervosa and Comorbid Depression: A Case Report

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ABSTRACT
The objective of this report was to describe an efficacious treatment of an adult with long-standing anorexia nervosa (AN). A 50-year-old woman with an over 7-year history of AN and comorbid major depression had been treated unsuccessfully with numerous psychotropic medications, manualized cognitive behavior therapy, and an intensive outpatient treatment program before referral. After treatment with mirtazapine, she gained weight and her depression improved. A 9-month follow-up revealed a maintenance of these benefits. Mirtazapine may be useful for older, chronically ill patients presenting with AN and comorbid depression. © 2010 by Wiley Periodicals, Inc.

Keywords: anorexia nervosa; mirtazapine; pharmacotherapy; eating disorders treatment; adults

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Introduction

Support for the effectiveness of pharmacotherapy for AN is lacking. While few rigorous randomized controlled trials have been conducted, overall there is no or at best mixed evidence for the use of antipsychotics such as olanzapine[1] or SSRIs such as fluoxetine[2,3] and no medications are approved by the Food and Drug Administration for the treatment of AN. To date, limited case studies[4,5] indicate that mirtazapine may be a promising choice for adolescents with AN and comorbid depression, but no reports are available on the use of mirtazapine in an adult with refractory AN.

Case Report

A 50-year-old married employed woman with a history of AN, depression, and anxiety was referred for a pharmacotherapy evaluation by her therapist for adjunctive treatment with psychotropic medications in the context of failure to gain weight and worsening depression. She recalled denying herself food ever since her teens and maintaining a body weight of about 90% of her ideal; but 7 years ago, she changed her eating habits "to get really healthy." She became "completely immersed in patterns of not eating." She lost over 11 kg in 3 months, eventually dropping to 34 kg (67% IBW, BMI = 15.4) and required hospitalization on a medical unit to stabilize her vital signs. This treatment was followed by 6 weeks of psychiatric treatment in an eating disorders intensive outpatient program. Since that point she had continued to struggle with her weight, not able to reach above 40.8 kg (85% IBW), thus continuing to meet AN criteria. Over this period, she received 2 years of weekly therapy followed by 5 years of monthly outpatient individual psychotherapy visits. This was followed by an additional year of weekly sessions and sporadic sessions with a nutritionist. She also was treated with medications (described in detail below) requiring monthly pharmacotherapy sessions. In addition, she participated in 1 year of regular outpatient group therapy. At the beginning of the current treatment regimen using manual-based Cognitive Behavioral Treatment for AN (CBT), she weighed 40.6 kg (84% IBW). While the patient reported that CBT was useful in helping her to identify and challenge distorted cognitions, it did not lead to weight gain (Fig. 1) and her depression worsened. The patient was then referred for a pharmacotherapy evaluation.

Initial Presentation

At the initial pharmacotherapy evaluation, the patient weighed 39.7 kg (82.9% IBW). She described severely restrictive eating patterns, allowing only very small portion sizes (e.g., 3–4 almonds or ½ sandwich) and engaged in excessive exercise to the

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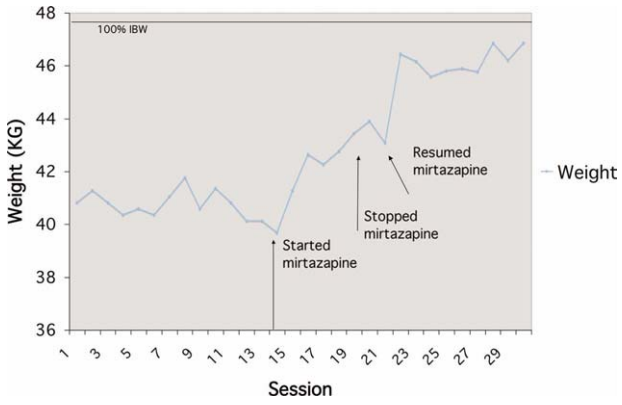
FIGURE 1 Weight progress of an adult with anorexia nervosa over the course of a 32-session treatment, showing psychotherapy and the addition of mirtazapine. Note: IBW = Ideal Body Weight. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]



point of exhaustion. She had an intense fear of becoming fat, a disturbed body image ("I see huge hips when I look in the mirror"), and found herself constantly preoccupied with thoughts about food and her food intake. The patient denied binge eating, though she did occasionally purge at a maximum frequency of about once per week.

In addition to AN, the patient had several comorbid psychiatric disorders. She reported a significant history of being depressed and anxious "all my life," with a suicide attempt at age 14 years. She was first diagnosed with major depression at the age of 40 when she began working with a psychotherapist using CBT for depression. The antidepressant medication paroxetine (20 mg QD) was added and within several months she experienced a complete remission. She stopped both psychotherapy and medications after 1 year, due to a long-standing dislike of being on medications. In the past, she had also been treated with sertraline. At the time of the current evaluation, she was taking escitalopram 10 mg QD (begun 1 year before); buproprion 150 mg BID (begun about 4–5 months before); alprazolam 2 mg QHS as needed for insomnia and 0.5 mg as needed for anxiety (begun about 2–3 months before). The patient stated that the medications were helpful but not optimal. While she denied ongoing sadness, she reported unstable mood. The patient noted the presence of suicidal ideation but denied a plan or intent. She had no symptoms consistent with mania.

Her social history included the divorce of her parents when she was 3 years old and a significant trauma history, including sexual molestation as a child, attempted rape at age 13, and a date-rape at age 17. She married in her early twenties and has 4 children. She currently works as a teacher. Her father suffered from alcoholism and depression and committed suicide. Her past medical history included migraine headaches and a duodenal ulcer. Habits include smoking 1–2 cigarettes/ day and occasionally drinking 1–2 glasses of wine per night.

On mental status exam, the patient was a well-groomed, very thin (but not emaciated) woman who looked much younger than her stated age. She was cooperative, exhibited a slightly restricted affect with linear thought processes. She endorsed passive suicidal ideation without intent or plan. There was no evidence of psychotic symptoms. On the basis of this history and evaluation, the patient met criteria for comorbid dysthymia, generalized anxiety disorder, and post traumatic stress disorder.

Treatment Course

Several medication changes were advised. The patient was to begin tapering off her escitalopram by initially decreasing by ¼ of a tablet (about 2.5 mg) as tolerated. Mirtazpine 30 mg qhs was to be started. The patient, when informed of the likely side-effect of weight gain, initially hesitated. However, after discussion emphasizing the chronicity of her AN symptoms and her lack of weight gain over many years, she agreed. In addition, the patient was informed that the majority of weight gain occurs during the first 4–12 weeks[6,7] and then tends to level off. Aiding the patient's acceptance of a mirtazapine trial was her dislike of sexual side-effects from her SSRI and her desire for mirtazpine's help with sleep and decreased anxiety. The patient was advised to discontinue her occasional use of alprazolam, especially given her impulsive tendency to combine it with alcohol; because of buproprion's contraindication in patients with a history of purging (due to the increased risk of a seizure), this medication was also discontinued.

At 2 week follow-up, the patient noted feeling her mood had improved. However, she said she felt a "ravenous" appetite and had gained 1.4 kg the week before. She also complained of initial tongue parasthesias and excess sleepiness. Overall, however, she felt comfortable on the medication was willing to continue.

The patient continued psychotherapy and was seen as needed (usually monthly or bimonthly) for medication management. Over the next 6 weeks, the patient gained a total of 4.2 kg (weight 43.9 kg, BMI = 19.9) (Fig. 1). During that time, her dose had been increased to 45 mg to target her episodic

remaining depressive symptoms. At the end of these 6 weeks, the patient felt well enough that she decided to self-discontinue her mirtazapine. During the 2 weeks off mirtazapine, her weight dropped by 0.8 kg and her eating disordered behaviors of restriction and preoccupation with food, depression, and anxiety worsened. Upon restarting mirtazapine, her weight increased again and her depression improved. A later attempt to decrease her mirtazpine from 45 mg to 30 mg several months later led to significant worsening of her mood and urges to engage in dietary restriction, leading her to resume the 45 mg dose. Over the following months, the patient's weight continued to increase (Fig. 1) until she reached 46.7 kg ((97% IBW, BMI = 21.2). She maintained this weight at 11 months follow-up.

Discussion

We present the first case report of an adult with refractory AN associated with major depression and significant anxiety who responded well to outpatient treatment of mirtazapine. There are no medications approved by the FDA nor evidence-based psychotherapy treatments for the treatment of AN. Mirtazapine was chosen because of it's demonstrated efficacy for depression and because mirtazapine might improve appetite and weight. The available literature on the off-label use of mirtazapine in AN, as identified via PubMed searches, was limited. Two reports on mirtazapine monotherapy with AN involved its use with adolescent patients.[4,5] A case report of an adult with AN was identified but this utilized the combination of mirtazapine and olanzapine.[8] Given the risk of tardive dsykinesia and absence of any psychotic symptoms, the decision was made to begin with mirtazpine alone.

Mirtazapine, an atypical antidepressant with noradrenergic and specific serotonergic activity, blocks alpha-2 autoreceptors and heteroreceptors (enhancing serotonin release), selectively antagonizes the serotonin 5-HT2 and 5-HT3 receptors in the central and peripheral nervous system, enhances serotonin neurotransmission at the 5-HT1 receptor, and blocks the histaminergic (H1) and muscarinic receptors.[9–11] The exact mechanism by which mirtazpine results in weight gain is unclear. One hypothesis is its relationship to 5HT2C and H1 antagonism[10] or possibly secondary changes in leptin and the tumor necrosis factor-alpha (TNF-alpha) cytokine system.[12] Weight gain is a major impediment to the use of mirtazapine, as well as many other psychotropic medications, in a population of patients with refractory AN. However, patients can be informed that the majority of weight gain occurs during the first 4 weeks of treatment[6] and is relatively stable by the 3rd month of treatment.[7] For example, a large study of mirtazapine for the prevention of depressive relapse by Thase et al. involved 8–12 weeks of open-label mirtazapine therapy followed by a double-blind continuation phase therapy with either mirtazpine or placebo.[7] The average medication related weight gain during the initial 3 months was 2.5 kg. Over 40 weeks of continued mirtazapine, the additional average weight gain was 1.4 kg on a dose of 15–45 mg [compared with a −1.7 kg change on placebo].[7] Generally, if weight gain is not problematic during the acute phase, it is unlikely to become so during longer-term treatment.

The authors present this case report to illustrate that mirtazpine may be a particularly suitable option for adults with chronic AN and comorbid depression whose symptoms had not responded to before medications or psychotherapeutic treatment. Indeed, few reports exist on adults who report an onset of anorexic symptoms over the age of 25.[13] This case report thus adds to a scarce literature. Without a controlled comparison (e.g., psychotherapy + placebo), one cannot determine if the patient's symptomatic improvement was due to continued psychotherapy alone. However, the coincidence in the timing of her improvement and worsening with the cessation of mirtazapine treatment suggest the influence of mirtazapine was central to her weight improvement. Further controlled trials of mirtazapine for AN with and without comorbid depression are needed to explore the role of mirtazpine in clinical practice.

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