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LETTER TO THE EDITOR

Mirtazapine and Weight Gain in Avoidant and Restrictive Food Intake Disorder

To the Editor:

Avoidant and restrictive food intake disorder (ARFID) is a newly classified disorder in the *DSM-5* that describes a pattern of restrictive eating across the lifespan that results in significant weight loss, nutritional deficiency, dependence on enteral feeding or nutritional supplements, or marked interference in psychosocial functioning.[1] Currently, there are no evidence-based treatment approaches or medications for this disorder.[2] We have administered a range of psychoactive medications to those with ARFID in our treatment program in an attempt to find an effective medication. One medication of interest has been mirtazapine because it promotes appetite and weight gain, decreases nausea and vomiting, and improves gastric emptying. Although mirtazapine is an off-label approach in a pediatric population and carries a black box warning for an increased risk of suicide, it is an effective treatment for depression and anxiety symptoms in adults and is generally well tolerated.[3,4] There are no studies to date reporting on the use of mirtazapine in patients with ARFID.

We performed a retrospective chart review of 14 sequential patients given mirtazapine in our clinic. Cases were identified from previous patients who met *DSM-5* criteria for ARFID and received treatment at the University of California, San Diego Eating Disorders Clinic from 2015 to 2016. Cases were selected if they included a clinical description of difficulty eating related to low appetite cues, taste, or texture sensitivity, anxiety of an adverse event (e.g., choking), or significant functional gastrointestinal distress. Cases were excluded if the patient had any history of purging, laxative use, excessive exercise, fear of weight gain, body checking behavior, or calorie counting. In addition to mirtazapine, all patients received treatment as part of a partial hospital program for the treatment of eating disorders and were on a weight restoration protocol. We used a dependent t test to compare the rate of weight gain within patients before initiation of mirtazapine and after initiation of mirtazapine. Rate of weight gain was calculated as the rate of change in body mass index (BMI) per week. We excluded 1 patient from this analysis because mirtazapine was initiated after the patient achieved weight restoration.

The 6 female and 8 male subjects were 7 to 23 years old (mean 15.2, standard deviation [SD] 5.5) and had a mean BMI at intake of 16.8 kg/m^2 (SD 1.6, range 13.9–19.1). The average length of treatment was 13.7 weeks (SD 5.2, range 7–25) and the mean discharge BMI was 19.5 kg/m^2 (SD 1.9, range 16.3–22.3). Thirteen patients were diagnosed with a current comorbid diagnosis by clinical interview including at least 1 of the following: generalized anxiety disorder, social anxiety disorder, unspecified anxiety disorder, attention-deficit/hyperactivity disorder, major depressive disorder; and 2 patients had an existing diagnosis of autism spectrum disorder. Six patients were treated with mirtazapine as monotherapy, and 8 patients (58%) were on additional medications (citalopram, sertraline, venlafaxine, amphetamine salts, methylphenidate, clonidine, olanzapine, and cyproheptadine). Only 2 patients had changes in other medications while on mirtazapine. In 1 case, olanzapine was initiated and increased to target mood. In the second case, venlafaxine was initiated and increased to target depression and anxiety.

Patients were in treatment for an average of 3.4 weeks (SD 2.7) before initiating mirtazapine and were on mirtazapine for an average of 9.8 weeks (SD 5.1), continuing on the medication through discharge with 1 exception (patient discontinued during the final week of treatment owing to an increase in night eating). The average dose of mirtazapine was 25.5 mg (SD 17.9, range 7.5–60). The average change in BMI per week before initiating mirtazapine was 0.10 BMI point per week (SD 0.08) and the average change in BMI per week after mirtazapine was 0.23 BMI point per week (SD 0.14). This difference was statistically significant ($t_{13} = -3.11$, $p < .05$). These results suggest that mirtazapine could facilitate a faster rate of weight gain in patients with ARFID.

The most common side effect was drowsiness and sedation, which occurred in 8 of 14 patients (58%), but was ameliorated with a dose increase and was not severe enough to warrant discontinuation. Other reported side effects included increased anxiety (n = 4, 29%). It is notable that the increased anxiety in 2 patients was associated with a higher dosage of mirtazapine (15 and 30 mg) and was resolved by decreasing the dosage (7.5 and 15 mg, respectively). Insomnia and increased appetite were the only other side effects and were reported by 1 patient and prompted the only discontinuation of mirtazapine.

Overall, mirtazapine was safe and well tolerated and was affiliated with a greater rate of weight gain compared with our treatment-as-usual weight restoration program. Although findings are confounded by issues such as a small sample and other treatments, these data support further study of mirtazapine as an adjunct to weight gain in ARFID.

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Disclosure: Drs. Gray, Chen, Menzel, Schwartz, and Kaye report no biomedical financial interests or potential conflicts of interest.

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