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Use of Pharmacologic Agents With Weight Gain Potential for Panic Disorder Amid the COVID-19 Pandemic

To the Editor: We compliment Bhatia et al¹ for their description of a case of panic disorder due to the news of the coronavirus disease 2019 (COVID-19) pandemic, which highlighted the importance of also focusing on the psychiatric aspect of care amid the unprecedented crisis. With this letter, we would like to raise the issue of weight gain associated with the use of pharmacologic agents for panic disorders, since it has recently been discovered that obesity may be one of the driving factors in the risk of acquisition of and severity of illness with COVID-19.²

The patient in this case¹ had been treated with paroxetine, a selective serotonin reuptake inhibitor (SSRI). SSRIs can have a clinically significant impact on the body weight of their users. The effect depends on the specific SSRI prescribed and the duration of treatment. While users of SSRIs for a short-term basis usually notice no appreciable effect on their body weight, short-term therapy is not clinically appropriate for most patients with panic disorder due to fear of relapse. Treatment with SSRIs for the long term, which is commonly used in patients with panic disorder, may result in weight gain. Weight gain from SSRIs may be due to improved appetite, increased carbohydrate craving, and changes in serotonin 2C receptor activity. Paroxetine, which was prescribed for the patient described in the case report,¹ may have the most noticeable effect on weight gain among the SSRIs, for which up to a 3.6% increment in baseline body weight has been described.³ It has also been previously reported that up to one-quarter of patients receiving paroxetine experienced clinically significant weight gain $\geq 7\%$.⁴

On the other hand, fluoxetine may be the least problematic SSRI with regard to body weight since it has been associated with weight loss.^{3,4} Furthermore, there is one additional disadvantage with the use of paroxetine compared to fluoxetine. Due to its short half-life and nonlinear rapid decline, paroxetine is associated with a high risk for antidepressant discontinuation syndrome in the case of abrupt discontinuation compared to fluoxetine, which is essentially free of such risk owing to its especially long half-life.⁵ Indeed, antidepressant discontinuation syndrome could include flu-like symptoms, fatigue, headache, and dyspnea, which may be confused with the symptoms of COVID-19.

Likewise, venlafaxine, which is a serotonin-norepinephrine reuptake inhibitor used for the treatment of panic disorder, has been associated with weight changes in both the short and long term. A pooled analysis⁶ of randomized trials and observational studies lasting 4 to 12 weeks suggested that short-term treatment with venlafaxine is associated with a weight loss of 0.5 kg. However, a retrospective study⁷ of 49 patients receiving venlafaxine for an average of 18 months reported a mean weight gain of 7 kg. Moreover, due to their actions on dopamine and histamine receptors, the 2

tricyclic antidepressants used for the treatment of panic disorder, namely imipramine and clomipramine, can also lead to weight gain.

The acknowledgment of the potential for pharmacologic agents for the treatment of panic disorder to cause significant weight gain will help in the appropriate selection and modification of pharmacologic therapy during the COVID-19 crisis, especially for patients who have other comorbidities such as diabetes and hypertension that put them at risk of COVID-19 acquisition. Fluoxetine may be particularly favored for the treatment of panic disorder with regard to body weight, but navigation to the right pharmacologic agent also depends on the patient's response to a particular agent. Clinicians involved in the management of panic disorder should also encourage therapeutic lifestyle changes to lose extra weight or prevent weight gain, especially amid the COVID-19 pandemic.

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Dr Bhatia and Colleagues Reply

To the Editor: In this case,¹ a detailed examination of the patient was conducted. The patient had no past medical history of hypertension, diabetes mellitus, thyroid dysfunction, or other medical illness. His body mass index was also noted, which was within normal limits. With all of these factors in mind, his medication was started in addition to psychotherapy. The patient presented for regular follow-up, and no side effect with paroxetine was observed or reported by the patient.

Fluoxetine is also associated with gastrointestinal side effects and activating effects, which result in noncompliance in patients. And, many patients with coronavirus disease 2019 (COVID-19) also present with gastrointestinal disturbance, which could have increased the patient's anxiety with regard to COVID-19. Although some selective serotonin reuptake inhibitors are associated with weight loss at first, long-term use (ie, > 6 months) is mostly linked to weight gain.² Weight gain is less likely with citalopram or sertraline compared to fluoxetine and paroxetine.^{3,4} Nausea and sweating are more common with fluoxetine, whereas other adverse effects are not statistically significant.⁵

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