Psychopharmacology for the Clinician
Psychopharmacologie pratique

The information in this column is not intended as a definitive treatment strategy but as a suggested approach for clinicians treating patients with similar histories. Individual cases may vary and should be evaluated carefully before treatment is provided.

Implementing antiobesity treatment in a patient with a mood disorder

Mrs. C is a 42-year-old woman with type 1 bipolar affective disorder. It has taken her 15 years, a battle with substance abuse and 3 hospital admissions, all owing to medication noncompliance, to achieve mood stability. She is currently well and takes a combination of lithium, atypical antipsychotic and selective serotonin reuptake inhibitor therapy. She initially took bupropion, but because of agitation she switched first to paroxetine and then to escitalopram. During those 15 years, Mrs. C gained 38 lbs, and her body mass index increased from 29.1 to 35.4 kg/m^2. Dyslipidemia developed, and, with a fasting blood glucose level of 6.3 mmol/L, Mrs. C was considered to be prediabetic. She felt her weight negatively impacted both her physical and psychological health, and she presented requesting treatment options.

A change in lifestyle with a focus on improved nutrition and increased physical activity is the cornerstone of any weight-management program. But for many people, lifestyle modification alone is not sufficient for weight loss, particularly when the problem is compounded by the weight-gain potential associated with psychotropic medication and a symptom profile that impacts energy level and appetite.

Two medications approved for long-term use in the treatment of obesity are available in Canada: sibutramine and orlistat. Sibutramine is a serotonin-noradrenaline reuptake inhibitor, and it is thought to work primarily by increasing satiety, with a mild increase in thermogenesis. Canadian labelling states that use of sibutramine with other centrally acting drugs for the treatment of psychiatric disorders, including antidepressants and antipsychotics, is contraindicated.[1] US labelling identifies only centrally acting weight-loss drugs and monoamine oxidase inhibitors as contraindications.[2] This warning relates to a potential drug interaction that can lead to serotonin syndrome or elevated blood pressure. Orlistat has no central mechanism of action and is a lipase inhibitor that has a dose-dependent effect on fecal fat loss; in diets comprising 30% fat, about one-third of the dose will not be absorbed. It has little effect in people with low-fat diets, and its mechanism of action, which can lead to gastrointestinal symptoms and oily stool, is not well tolerated by some patients.

After evaluating both treatments, Mrs. C decided to try sibutramine. We discussed the symptoms of serotonin syndrome and the need to be cautious with products such as grapefruit juice or erythromycin. These compounds can inactivate cytocrome P450 3A4, a key component in the metabolism of sibutramine and escitalopram, resulting in an increase in the level of both medications. We discussed the potential for antidepressant-induced mania, addressed the use of off-label treatment and devised a plan to regularly monitor Mrs. C's blood pressure at her family physian's office. The use of off-label treatments is not uncommon, but it is important that the risks and benefits are explained to patients, as well as the rationale behind the treatment choice.

Three months after starting sibutramine, Mrs. C had lost 7 lbs, and her fasting blood glucose level improved. Although she felt hopeful, she was frustrated that the changes were not more substantial. Both sibutramine and orlistat produce on average a 10% decrease in excess body weight and require long-term use, since discontinuing the medication results in weight regain for most people. Although both drugs work differently, there is little advantage to taking them simultaneously.[3] We discussed realistic outcomes and goals with Mrs. C and referred her to a dietician.

Weight management is difficult in the general population, and it becomes even more complicated for individuals taking psychotropic medications. Sibutramine has been used successfully to manage olanzapine-induced[4] weight gain in patients with schizophrenia; however, it was less successful with clozapine-induced weight gain in a similar population.[5] It has been shown to be a weight-loss agent comparable to topiramate in the bipolar population, although tolerability is a concern with both medications.[6] Mrs. C experienced cognitive dysfunction with topiramate but was able to tolerate sibutramine.

Although no perfect treatment of weight gain in bipolar patients exists, medications that are not taken cannot work. Given that weight gain is an important contributor to medication noncompliance, it is not an issue that can be ignored. This case illustrates that we do have options, but it also outlines how diligently we must monitor patients prescribed antiobesity medications.

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Competing interests: Dr. Taylor has consulted for Sanofi Aventis, and she has received speaker fees and sits on the advisory boards of Sanofi Aventis and Astra Zeneca.

References

1. Meridia [package insert]. Saint-Laurent (QC): Abbott; 2005.

Psychopharmacology for the Clinician columns are usually based on a case report that illustrates a point of interest in clinical psychopharmacology. They are about 500–650 words long and do not include references. Columns can include a bibliography which will be available only on the journal website and can be accessed through a link at the bottom of the column.
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2. Meridia [package insert]. Chicago (IL): Abbott; 2005.
3. Wadden TA, Berkowitz RI, Womble LG, et al. Effects of sibutramine plus orlistat in obese women following 1 year of treatment by sibutramine alone: a placebo-controlled trial. *Obes Res* 2000;8:431-7.
4. Henderson DC, Copeland PM, Daley TB, et al. A double-blind, placebo-controlled trial of sibutramine for olanzapine-associated weight gain. *Am J Psychiatry* 2005;162:954-62.
5. Henderson DC, Fan X, Copeland PM, et al. A double-blind, placebo-controlled trial of sibutramine for clozapine-associated weight gain. *Acta Psychiatr Scand* 2007;115:101-5.
6. Baptista T, Uzcategui E, Rangel N, et al. Metformin plus sibutramine for olanzapine-associated weight gain and metabolic dysfunction in schizophrenia: a 12 week double-blind, placebo-controlled pilot study. *Psychiatry Res* 2008;159:250-3.