

Use of Lorcaserin, A 5HT_{2C} Agonist, In the Management of Olanzapine-Induced Weight Gain

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Abstract

Atypical antipsychotics are associated with weight gain, which compromise medication adherence and pose long-term health complications. These are two cases in which lorcaserin, a 5HT_{2C} agonist, has been used to counteract olanzapine-induced weight gain in conjunction with a low carbohydrate diet. In Case 1, patient lost a significant amount of weight and reported decreased food cravings. In Case 2, patient showed initial response but was unable to maintain diet. Patient had significant weight gain and reported increased cravings after discontinuing lorcaserin. These cases demonstrate 5HT_{2C} agonists' potential for management of atypical antipsychotic-related weight gain.

Keywords: Lorcaserin; Weight gain; Atypical antipsychotics; Olanzapine; Metabolic syndrome; Complications

Introduction

Weight gain is a common side effect associated with antipsychotics, particularly atypical antipsychotics. This poses a number of challenges to successful treatment, including medical complications of metabolic syndrome as well as potential for decreased adherence due to this unwanted side effect. Weight loss is achieved by decreasing caloric intake, not increasing energy expended, therefore medications reducing food cravings and promoting feelings of satiety could be a valuable tool for helping patients with antipsychotic-induced weight gain.

Exactly how antipsychotics contribute to weight gain is not fully understood, but their antagonism of the 5HT_{2C} receptor has been linked to increased propensity for weight gain. The 5HT_{2C} receptor modulates activity in the hypothalamic proopiomelanocortin neurons, which influence perception of satiety. 5HT_{2C} agonism decreases food cravings and increases feelings of fullness. Mice models missing these receptors were more likely to be obese, whereas mice models with increased expression of these receptors had decreased food intake and lower body weights compared to controls. 5HT_{2C} modulation appears to be an important modulator of obesity particularly in high-fat diets as opposed to leptin-based modulation, which plays a more prominent role in obesity when subjects follow a carbohydrate-rich diet [1-5].

Lorcaserin is a selective 5HT_{2C} agonist, FDA-approved for adult weight management in conjunction with low-calorie diet and exercise regimen. It was hypothesized in the following two case studies that lorcaserin's agonist activity may counteract the 5HT_{2C} antagonism of olanzapine, helping to reduce appetite, and aid weight loss in patients that have experienced significant weight gain as a result of this psychotropic medication.

Case Presentation

Case 1

A 29 year old Asian male with schizophrenia on risperidone long-acting injectable 50 mg every 2 weeks and divalproex 1500 mg at bedtime started olanzapine 10 mg at bedtime for persistent psychotic symptoms. Six months after starting olanzapine, patient had gained 62 pounds, with total weight 272 pounds (BMI 41.1). Lorcaserin 10mg bid was added and the patient was educated to follow a low carbohydrate diet. The patient didn't report any adverse events. Three months after starting lorcaserin 10mg bid, patient weighed 245.8 pounds,

representing 9.6% weight loss (26.2 pounds). Patient's food cravings, as measured by the Food Cravings Inventory (FCI) decreased 50.5% compared to baseline. His fasting insulin level was 61.6 (baseline fasting insulin level wasn't obtained) (Table 1).

Case 2

A 35 year old Hispanic male with schizophrenia on risperidone 4 mg at bedtime started olanzapine 10 mg at bedtime for uncontrolled psychotic symptoms. Four months later, patient gained 26 pounds, with total weight 221 pounds (BMI 31.7). One week after starting lorcaserin 10 mg bid, patient lost 5 pounds and reported 21% reduction in food cravings by FCI. Patient was unable to maintain low-carbohydrate diet; his weight increased to 225.6 pounds twelve weeks after he started treatment (2.1% increase compared to weight prior to starting lorcaserin). Lorcaserin was subsequently discontinued due to lack of response in accordance with the label. Six weeks after discontinuing lorcaserin, patient weighed 234.6 pounds (4% gain from weight at discontinuation) as well as 28% increase in food craving. As a result, the olanzapine was discontinued at that time (Table 2).

	Initial	3 months later	14 months later
Chol	182	133	151
HDL	37	27	35
Triglyceride	434	223	138
LDL	93	61	88
HbA1C	5.7	4.6	5.3
Insulin	None	61.6	6.5
AST	47	None	18
ALT	46	None	20
Weight	272	245.8	225.8

Table 1: Case 1.

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	Initial	3 months later	12 months later
Chol	215	None	176
HDL	53	None	43
Triglyceride	180	None	194
LDL	126	None	94
HbA1C	5.7	None	5.8
AST	None	None	32
ALT	None	None	39
Weight	221	225.6	229.4

Table 2: Case 2.

Treatment

Both patients were initiated on lorcaserin 10 mg twice a day and instructed to follow a low carbohydrate diet.

Outcome and Follow-Up

Case 1: The patient continued treatment with lorcaserin for a total of 14 months. He lost another 20 pounds, weighing at 225.8 pounds. His AST and ALT improved as well as his cholesterol, triglycerides, HDL, and LDL. His fasting insulin normalized at 6.5.

Case 2: After stopping the olanzapine, the patient reported feeling less hungry. He didn't gain any more weight and was able to lose about 5 pounds. Twelve months after he started lorcaserin, the patient weighed 229.4 pounds. His cholesterol, triglycerides, HDL and LDL improved.

Discussion

While lorcaserin is FDA-approved for chronic weight management in adults, it has not been studied specifically in populations dealing with antipsychotic-induced weight gain.

The patient in Case 1 demonstrated a substantial decrease in food cravings as well as clinically significant weight loss (9.6% weight loss). The patient attributed the decrease in food cravings to helping him follow the low carbohydrate diet. The patient had significant reduction in his fasting insulin level. The mechanism of improvement is unknown, but we postulate that a change in diet may be a huge contributing factor.

The patient in Case 2 initially showed a similar response; however, he ultimately was unable to follow the low-carbohydrate diet and continued to gain weight. The patient didn't have stable housing so he was unable to cook his own meals. He ate at soup kitchens or fast foods that contained starchy carbohydrates. Even though the patient didn't have as much food cravings, his limited food choices led him to eat high caloric foods. In addition, the patient admitted to medications noncompliance due to his unstable living situation. This may have contributed to an increase in food cravings, leading to weight gain.

It is noteworthy, however, that patient's had gained more weight after discontinuing lorcaserin than he did while taking this medication (4% increase after discontinuing medication versus 2.1% increase while

taking lorcaserin). He also reported increased food cravings while off the medication while he was still taking olanzapine. After olanzapine was discontinued; the patient reported fewer cravings and was able to lose some weight on his own.

There were multiple factors contributing to patient's continued weight gain in case 2. Patient's inability to adhere to the recommended diet was likely a major contributing factor, but it is important to note that olanzapine acts on receptors other than 5HT2C that are also associated with appetite and weight. Olanzapine has strong antagonist activity at the histamine-1 receptor, which has been correlated to weight gain. Olanzapine has antagonistic activity at peripheral M3 muscarinic receptor, which has been shown to have a dose-dependent connection to obesity [6]. Further exploration of these mechanisms may help identify which patients will benefit most from interventions like lorcaserin.

The results in these two cases suggest that Lorcaserin's selective 5HT2C agonist properties can counteract olanzapine's 5HT2C antagonism, resulting in increased satiety. This has implications for facilitating weight loss or at the least, mitigating weight gain while taking olanzapine.

Conclusion

- Lorcaserin has potential as an effective treatment to reduce food cravings and facilitate weight loss in patients experiencing olanzapine-induced weight gain.

- Although lorcaserin yielded promising initial results in case 2, patient's inability to adhere to diet suggests that other mechanisms contributing to weight gain must continue to be explored.

- The proposed mechanism by which lorcaserin facilitates weight loss is that its agonist effect counteracts olanzapine's antagonistic effect on 5HT2C receptors.

References

1. Prahara SK, Jana AM, Goyal N (2011) Metformin for olanzapine-induced weight gain: a systematic review and meta-analysis. *Br J Clin Pharmacol* 70: 377-382.
2. Wu R, Zhao J, Jin H (2008) Lifestyle Intervention and Metformin for treatment of antipsychotic induced weight gain, A randomized controlled trial. *JAMA* 299: 185-193.
3. Alvarez-Jimenez M, Gonzalez-Blanch C, Vazquez-Barquero JL, Pérez-Iglesias R, Martínez-García O, et al. (2006) Attenuation of antipsychotic induced weight gain with early behavioral intervention in drug-naive first-episode psychosis patients: a randomized controlled trial. *J Clin Psychiatry* 67: 1253-1260.
4. Allison DB, Mentore JL, Heo M, Chandler LP, Cappelleri JC, et al. (1999) Antipsychotic-induced weight gain: a comprehensive research synthesis. *Am J Psychiatry* 156: 1686-1696.
5. Kirk S, Glazebrook J, Grayson B (2009) Olanzapine-induced weight gain in the rat: role of 5-HT2C and histamine H1 receptors. *Psychopharmacology* 207: 119-125.
6. Smith SR, Weissman NJ, Anderson CM, Sanchez M, Chuang E, et al. (2010) Multicenter, placebo-controlled trial of lorcaserin for weight management. *N Engl J Med* 363: 245-256.