COMMENTARY

Lorcaserin: Making headway

Cynthia Gershome

ABSTRACT

Obesity is a global problem which has reached epidemic proportions. Obesity is morbidly associated with metabolic syndrome, type-2 diabetes, cardiovascular disease and increased cancer risk. There is an alarming increase in the incidence of obesity in young children which puts them at a greater risk for developing diseases at a much earlier age. Obesity also imposes a heavy burden on the healthcare system. Lorcaserin, a novel anti-obesity drug, is a selective agonist to 5-HT\textsubscript{2C} receptors thereby reducing food intake and promoting weight loss. Lorcaserin has 15-times and 100-times higher selectivity for the 5-HT\textsubscript{2C} receptor compared to the 5-HT\textsubscript{2A} and 5-HT\textsubscript{2B} receptors, respectively.

Keywords: Obesity, novel therapies, lorcaserin, weight loss

Introduction

Obesity is a global problem which has reached epidemic proportions. Obesity is morbidly associated with metabolic syndrome, type-2 diabetes, cardiovascular disease and increased cancer risk. There is an alarming increase in the incidence of obesity in young children which puts them at a greater risk for developing diseases at a much earlier age. Obesity also imposes a heavy burden on the healthcare system.

Effective intervention for the treatment of obesity is bariatric surgery which involves invasive procedures and carries significant risks.

Reducing caloric intake and leading an active lifestyle through regular exercise although is the best alternative but to achieve significant results takes motivation and commitment over a long time course. Anti-obesity drugs are thus an important intervention as a short term treatment option to patients who are morbidly obese with complications and have restricted abilities to perform physical activity. Current anti-obesity drugs approved by United States Food and Drug Administration (USFDA) include phentermine, phentermine/topiramate (Qsymia) and lorcaserin.

Obesity and the serotonin system

Serotonin has a pivotal role in the satiety and control of food intake. Various serotonin/5-hydroxytryptamine (5-HT) receptors have been identified and of these, 5-HT\textsubscript{2} subfamily is a target for many anti-obesity drugs. 5-HT\textsubscript{2} receptor subfamily includes 5-HT\textsubscript{2A}, 5-HT\textsubscript{2B} and 5-HT\textsubscript{2C}. 5-HT\textsubscript{2C} receptors are exclusively located in the central nervous system and are involved in the suppression of appetite. This vital role in appetite control makes 5-HT\textsubscript{2C} as a promising anti-obesity target. However, due to highly conserved amino acid sequence between the 5-HT\textsubscript{2} receptor subfamily, developing highly 5-HT\textsubscript{2C} selective drugs has been a challenging task. Non-selective 5-HT drugs have been shown to reduce body weight but had serious side effects owing to their activation of 5-HT\textsubscript{2A} and 5-HT\textsubscript{2B} receptors.

Lorcaserin – the new entrant

Lorcaserin, a novel anti-obesity drug, was approved by FDA in June 2012, marketed by Arena Pharmaceuticals (San Diego, CA) under the trade name Belviq. Chemically lorcaserin is [(1R)-8-chloro-1-methyl-2, 3, 4, 5-tetrahydro-1H-3-benzazepine hydrochloride hemihydrate] and is a selective agonist to 5-HT\textsubscript{2C} receptors thereby reducing food intake and promoting weight loss. Lorcaserin has 15-times and 100-times higher selectivity for the 5-HT\textsubscript{2C} receptor compared to the 5-HT\textsubscript{2A} and 5-HT\textsubscript{2B} receptors, respectively.

Lorcaserin is prescribed along with a low-calorie diet and regular physical activity for obese patients who have Body Mass Index (BMI) of 30 kg/m\textsuperscript{2} or overweight patients with BMI of 27-30 kg/m\textsuperscript{2} and also have one of the obesity related conditions such as type-2 diabetes, high cholesterol or hypertension.

Lorcaserin – the evidence

Three clinical trials have been published so far evaluating the efficacy and safety of lorcaserin for weight loss in obese population: Behavioral modification and lorcaserin for overweight and obesity management (BLOOM), behavioral modification and
lorcaserin for overweight and obesity management in patients of diabetes mellitus type 2 (BLOOM DM) and behavioral modification and lorcaserin second study for obesity management (BLOSSOM). For the BLOOM and BLOSSOM trials, obese or overweight patients were randomized to receive either placebo or lorcaserin 10 mg twice daily for 52 weeks. BLOOM-DM had a similar study design but involved obese patients with type 2 diabetes. These 3 clinical trials demonstrated effective weight loss of ≥ 5-10% in lorcaserin treated obese patients compared to placebo and also demonstrated a positive outcome on glycated hemoglobin levels, fasting blood glucose, decrease in blood pressure and BMI along with weight loss in obese patients with type-2 diabetes. Meta-analysis of pooled data from five clinical trials show that lorcaserin caused a modest reduction in the body weight but also caused significant side effects including headache, dizziness, nausea, upper respiratory tract infections and nasopharyngitis. FDA-defined mitral regurgitation (valvulopathy) side effect also developed in 2.7% of lorcaserin treated patients compared to 2.3% in placebo treated patients although statistically not significant. Other adverse side effects include depression and serotonin syndrome, when lorcaserin is used in combination with other serotonergic drugs such as serotonin-norepinephrine reuptake inhibitors, monoamine oxidase inhibitors, antipsychotics to name a few.

Concluding remarks

Obesity is a growing health concern across the globe. FDA approval of lorcaserin is a significantly exciting step towards the treatment of obesity. However, large randomised clinical trials in comparison with other anti-obesity drugs are needed to address the benefit to risk ratio for the use of lorcaserin.

Conflict of interest

Dr. Gershome is an editorial advisory board member of Diabesity.

References


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