CLINICAL VIGNETTE

Inpatient Use of GLP-1R Agonists for Weight Loss Prior to Transplantation

Michael C. Garcia, MD and Dave Garg, MD

Introduction

Lung transplantation has become an effective treatment for patients with end-stage lung disease. However, despite advances, lung transplantation-related morbidity and mortality is still significantly higher than for other solid organ transplants.[1] Preoperative nutrition and weight are important. When stratified by degree of obesity, mortality risk increases for patients with a body mass index (BMI) > 35 kilogram (kg)/m^2. These patients are required to lose weight prior to transplantation as the magnitude of pre-transplant weight loss directly correlated with improvements in post-transplant survival.[1] We describe a patient with chronic respiratory failure who was started on a glucagon-like peptide-1 receptor (GLP-1R) agonist while hospitalized given need for expedited inpatient weight loss to be eligible for urgent lung transplantation.

Case

A 51-year-old female with obesity, rheumatoid arthritis complicated by chronic hypoxemic respiratory failure due to interstitial lung disease and pulmonary hypertension, type 2 diabetes, and hypertension, was admitted to the intensive care unit for progressively worsened shortness of breath. She required 10 liters (L) of supplemental oxygen at rest prior to admission and had minimal ability to ambulate.

At admission, she required high flow nasal cannula of 50 L/minute, FiO2 60%. Her weight was 98.6 kg, with BMI of 37.25 kg/m^2. Initial laboratory tests included hemoglobin A1c 8.0%, BUN 18 mg/dL, and creatinine 0.43 ml/dL.

In addition to pulmonary hypertension therapies including inhaled nitric oxide, sildenafil, and ambrisentan, she was treated with high-dose steroids and intravenous diuresis. Her clinical status was dire as her elevated BMI precluded her from transplantation, which was the main contraindications raised at the initial transplant committee review. Shortly following admission, we prescribed a calorie restricted meal plan consisting of protein shake for two meal replacements and one food meal which was carbohydrate controlled, with <2 grams (g) sodium. The protein target was at least 1.2 g/kg/day. Because of her critical status and urgent need for transplantation, we also started a medication to aid with weight loss as an adjunct to caloric restriction. A GLP-1R agonist was the safest option based on her cardiopulmonary status and hemodynamics. Liraglutide was started, with initial delay due to authorization requirement for inpatient administration. The patient started at the initial 0.6-milligram (mg) daily dose, which was titrated weekly until she reached 2.4 mg. She only received one dose of 2.4 mg, as she had rapid clinical decline secondary to lung disease and was transitioned to comfort care prior to her death.

During her admission, the patient had an episode of acute kidney injury that resolved prior to the start of liraglutide. Basal insulin dosing was adjusted after the start of liraglutide and further modified based on steroid dosing and weight change. She did not have any recognized side effects secondary to liraglutide. Over the 22-days following the initiation of liraglutide, she had a weight loss of 5.6 kg, as shown in Figure 1.

Discussion

Organ transplantation is becoming increasingly feasible, although strict criteria must be met to be considered a candidate. Multiple studies have shown that BMI may uniquely affect post-transplantation mortality, with each unit increase in BMI above 26 kg/m^2 associated with progressively higher mortality risk after lung transplantation.[2] The International Society for Heart and Lung Transplantation consensus statement recommends a BMI 30-34.9 kg/m^2 as a relative contraindication and BMI $\geq$ 35 kg/m^2 as an absolute contraindication to lung transplantation.[3]

Many patients with progressive lung disease have a higher likelihood to develop obesity due to chronic corticosteroid exposure and limited exercise capacity. The rate of obesity has steadily increased nationally and globally, and current trends suggest this will continue in the coming years.[4,5] Thus, in the future, patients' BMI may become an increasing barrier to transplantation, with increasing need for expedited weight loss, particularly in those patients too ill to leave the hospital.

GLP-1R agonists have quickly become a mainstay of outpatient type 2 diabetes management. Part of this stems from their ability to effectively reduce blood sugars and decrease insulin resistance via increased insulin secretion and synthesis and decreased glucagon release. Another reason increased popularity is their multiple other benefits. GLP-1R agonists will cause mild natriuresis in the kidney, increase contractility and heart rate and have vascular protective effects.[6] GLP-1R agonists are now recognized as powerful agents for the management of obesity and fatty liver through their ability to reduce appetite,

reduce gastrointestinal motility, and increase lipolysis in adipocytes.[7,8]

More recent literature supports the potential use of GLP-1R agonists in hospitalized patients for inpatient management of diabetes.[9] However, our case is one of the first to utilize GLP-1R agonists for the purpose of inpatient weight loss to help a critically ill patient qualify for transplantation. While the patient unfortunately died prior to transplantation, she was able to tolerate moderate titrated doses of liraglutide long with a very low calorie without any adverse side effects and good short-term results. More research is necessary regarding the use of GLP-1R agonists in the inpatient setting for the purpose of weight loss, especially as the need for inpatient weight loss becomes more common in the future.

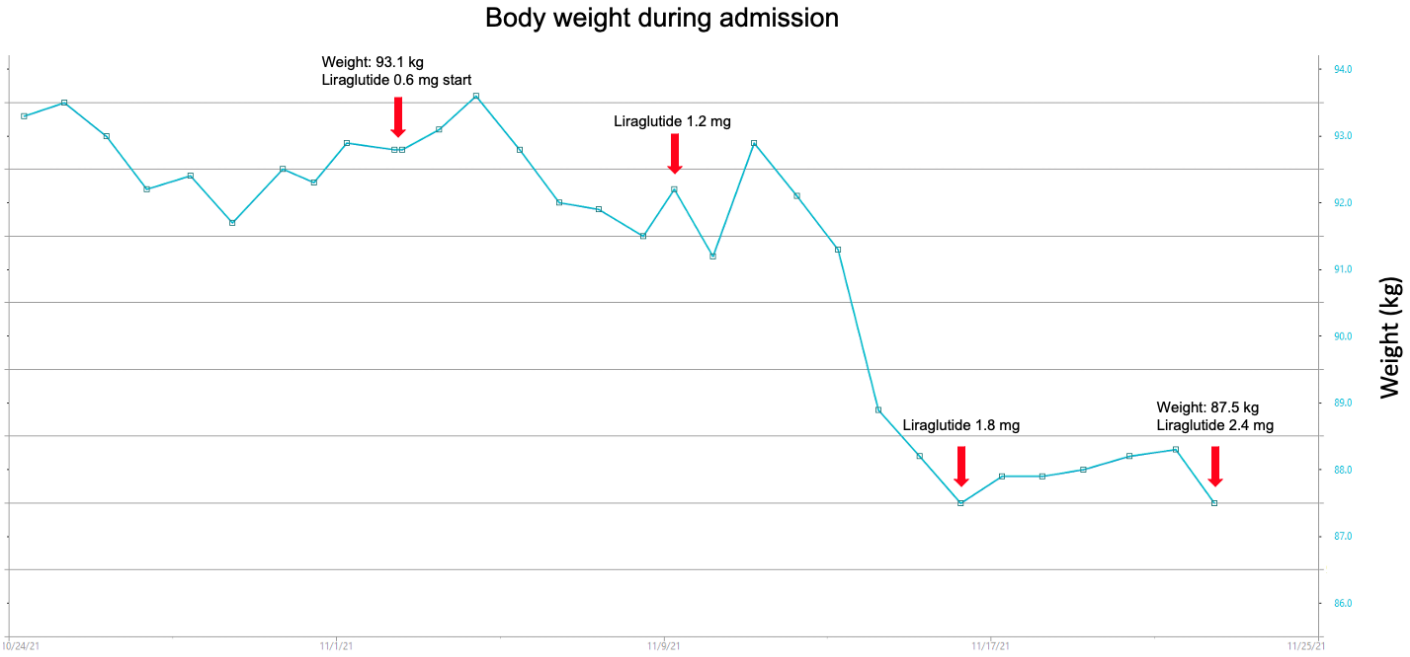

Figure 1: Effect of Daily Liraglutide on Body Weight
Change in body weight over time during entire admission period, with initiation and weekly dosage changes of liraglutide as marked.

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