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Liraglutide versus Semaglutide: Long Term Weight Loss Management in Obese Individuals

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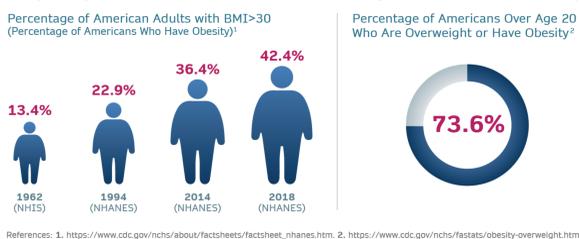
Abstract

Obesity has been a source of complications affecting multiple aspects from a physiological and psychological standpoint which has been steadily growing. There are a multitude of weight loss programs and medications with the idea of sustaining consistent weight loss to include use of the pharmaceuticals discussed within this review. The purpose of this literature review is to compare the efficacy and safety with use of liraglutide versus semaglutide (GLP-1 receptor agonists) in respect to long term weight loss management while in conjunction to lifestyle modifications within the obese population. Thorough research has been done with the aid of health science databases to include PubMed, ClinicalKey, and EBSCO. All of the studies were published between the year 2014 to 2022 and utilized human subjects greater than or equal to 18 years of age with specificity to subjects who were classified as “obese” based on their body mass index (BMI). The studies which were used throughout this review were composed of randomized control studies and systematic reviews. The data presented shows that both pharmaceuticals represented significant weight loss compared to their corresponding placebo, however concrete evidence was discovered that semaglutide was noted to be superior in compared to liraglutide in the form of weight loss management in obese individuals. Furthermore, the current research that is available and studied does not conclusively provide enough evidence nor has been studied properly when considering long term use of these pharmaceuticals.

Introduction

- The obesity epidemic is termed as a global and multifactorial disease resulting from a combination of genetic and environmental factors in association to several comorbid complications,
- As defined by the World Health Organization in 2016, approximately 1.9 billion adults, who are 18 years or older, were deemed as overweight and 650 million adults were deemed as obese (Shah, et al. 2014).
- Several studies that investigated the mechanism of action of GLP-1 receptor agonists found evidence that GLP-1 receptors are located in the hypothalamus which is involved with the regulation of food intake.
- Acute administration of these agents resulted in reduced feelings of hunger secondary to an increase in functional connectivity of the nucleus tract thus reducing energy intake and facilitating weight loss (Ard, et al. 2021).

Majority of Americans are Overweight or Have Obesity



Statement of the Problem

The prevalence of obesity continues to increase despite the use of several approved anti-obesity medications secondary to a multitude of factors to include lack of proper therapy, poor uptake and usage of therapy, adverse effects, and poor compliance. This has been characterized as a rising epidemic with no specific cure to the disease associated with high rates of relapse. Research has further proven the effects of pharmaceutical agents in conjunction to lifestyle modifications and weight management, but long-term use is in question.

Research Question

In comparing GLP-1 Receptor Agonist pharmaceuticals, **liraglutide** vs. **semaglutide**, what is the efficacy and safety of use for obese individuals with a BMI (Body Mass Index) greater than or equal to 30 kg/m² in long term weight management in conjunction with lifestyle modifications?

Literature Review

Overview of Liraglutide in the use of weight management

- Pi-Sunyer, et al. (2015) conducted a 56-week, randomized, placebo-controlled, double-blind trial that was aimed to evaluate the use of 3.0 mg once-daily subcutaneous injection of liraglutide.
 - A total of **63.2%** of patients in the Liraglutide group compared to **27.1%** in the placebo group lost at least 5% of their body weight from baseline (p<0.001), and **33.1%** and **10.6%** lost more than 10% of their body weight from baseline (p<0.001).

Safety and Efficacy of Liraglutide

- Two clinical trials, lasting 56 weeks, were conducted by le Roux, et al. (2017) that consisted of a randomized, double-blind, placebo-controlled, multicenter trials that sought out to investigate whether the efficacy and safety of liraglutide 3.0 mg injection differed between two subgroups of individuals
 - No associated difference** in the treatment efficacy or safety profile of liraglutide 3.0 mg.
 - Liraglutide 3.0 mg can be a considered pharmaceutical agent for treatment across the higher and lower classes of obesity in association to lifestyle management.

Overview of Semaglutide in the use of weight management

- A 68-week trial performed by Davies, et al. (2021) analyzed weight management and loss with the use of GLP-1 analogue, semaglutide compared to placebo.
 - At least 5% of participants baseline body weight was lost by **69%** of patients who were receiving **semaglutide 2.4 mg** dose in compared to **57%** **semaglutide 1.0 mg** and **28%** placebo.
 - Semaglutide 2.4 mg was effective in improving cardiometabolic risk factors as well as glycemic control in individuals with type 2 diabetes mellitus.

Safety and Efficacy of Semaglutide

- An observational, retrospective study was performed by Pérez-Belmonte, et al. (2022), on obese patients (body mass index greater than 30 kg/m²) who had underlying chronic heart failure to observe the use of subcutaneous semaglutide injections in conjunction to lifestyle modifications and weight loss management.
 - KCCQ score** which increased from **59.0 points** to **79.9 points** (p<0.01) as well as a reduction of patients **NYHA functional class** from **40.4% to 16.2%** (p<0.01).
 - Patients with a <7% HbA1c increased from **16.2%** at baseline to **64.5%** at 12 months (p<0.001). The evaluation of weight loss noted a significant reduction of body weight (12.7 kg) and BMI (7.1 kg/m²) with a decline in the proportion of patients with obesity to **50.8%**.

Direct comparison of Liraglutide vs. Semaglutide regarding efficacy and safety for weight management

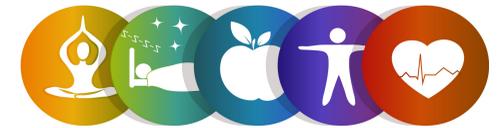
- Rubino, et al. (2022) conducted a 68-week long randomized trial that evaluated a comparison of liraglutide vs. semaglutide with respect to weight loss in overweight or obese adults.
 - The proportions of participants achieving 10% or more, 15% or more and 20% or more weight loss were **70.9%**, **55.6%** and **38.5%** with semaglutide, and **25.6%**, **12%** and **6%** with liraglutide.

Discussion

- Most adverse events were primarily localized to the gastrointestinal system to include nausea, vomiting, diarrhea, constipation, and abdominal pain were the most common symptoms verbalized from participants. Predominantly with semaglutide, the effectiveness and safety of the medication with dosage escalation was inconsistent across all trials. There was no dose dependency regardless of dose-escalations and the effect on the safety profile throughout the weeks of trial (O’Neil, et al. 2018).
- Long term use and safety of these pharmaceuticals, especially if it has been elected by the provider to keep individuals on these medications long term for weight loss management or other comorbid reasons, must be determined. Further trials and evaluation are needed to be performed and assessed in the future.
- Analyzing the efficacy of liraglutide, it was shown to be superior when compared to placebo with an average mean weight loss of 6.3-8.0% from baseline body weight across all trials.
- In considering semaglutide and its efficacy with weight loss management, it was found to be significantly superior compared to placebo throughout all trials within this project. A mean weight change across all literature analyzed was noted to be between 7.9-17.4% weight loss from baseline body weight. Studying semaglutide specifically and the dosage of the medication vs. weight loss, it was found that participants lost more weight at a consistent dose of 2.4 mg versus 1.0 mg.
- A direct comparison between liraglutide and semaglutide had shown favor towards semaglutide particularly for its effectiveness with weight management, but also for its favorable decrease in further cardiometabolic factors. Both pharmaceuticals were shown to be more effective with weight loss at higher dosages in conjunction to lifestyle modifications, however significant findings of dosing patterns were found with the semaglutide group specifically.
- Both pharmaceuticals had shown reductions in cardiometabolic risk factors to include waist circumference, blood pressure, fasting lipids, improved glycemic control, and inflammatory markers regardless of diabetic status.
- Participants apart of the semaglutide group was preferred over liraglutide regarding administration of the medication. This represented an increase in adherence from patients which ultimately provided better data when investigating the efficacy and safety of use.
- To ensure these medications may be used for an extended period as well as are safe and effective, it was determined through a majority of trials that long-term studies and clinical trials are needed to be implemented to further answer this question.

Applicability to Clinical Practice

- It should be considered that initiating these pharmaceuticals to an obese individual may be aiding in the sole aspect of weight loss; however, this may also lead to managing further underlying comorbid conditions such as hypertension, type 2 diabetes, and other various metabolic syndromes.
- It has been determined via literature analyzed for this comprehensive review, as well as first-hand accounts with professionals within this field that long term data is still needed.
- A secondary confrontation that has been addressed is insurance coverage of these pharmaceuticals, particularly for weight loss purposes. With up-and-coming medications that have been found to be superior in the sole aspect of weight loss such as semaglutide injectables, it has been difficult to have these medications approved for their own reasons, let alone for the linear purpose of weight loss.
- Physician associates can apply current practices and find out what may work best individually per patient through a consistent and measured approach and further resources they can utilize to ultimately achieve their goals for their health and overall well-being, whether that be with or without the use of pharmaceuticals.



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