

## Role of Semaglutide in Weight loss

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### Abstract

Obesity is a global health challenge with few pharmacologic options. Whether adults with obesity can achieve weight loss with once weekly Semaglutide at a dose of 0.5-1.0 mg as an adjunct to lifestyle intervention has not been confirmed. **Method:** This is a clinical case report of a 29-year-old female, who tried weekly Semaglutide with lifestyle intervention. We conducted a baseline mental and physical health, and we did a biweekly follow up with her. This was over 6 months period starting from September 2022 until March 2023. **Consent:** Written informed consent has been obtained from the patient. **Results:** Our participant was able to lose 16.3 % of her body weight in 6 months, dropping her body weight from 74.3 kilograms to 61.2 kilograms, with a decrease in her body mass index from 29.3 to 23.9. With a significant improvement in mental and physical health, particularly, an improvement in her depression, generalized anxiety, and ADHD symptoms. **Conclusion:** In participants with overweight or obesity, 0.5-1.0 mg of Semaglutide once weekly plus lifestyle intervention was associated with sustained, clinically relevant reduction in body weight.

**Keywords:** Obesity; Semaglutide; weight loss

### Introduction

Obesity is a chronic, multifactorial, and relapsing disease. Its medical burden includes multiple comorbidities, such as type 2 diabetes, hypertension, dyslipidemia, stroke, coronary heart disease, and various cancers. Considering the medical and economic costs associated with obesity, effective weight management is important to mitigate the associated morbidity and mortality.

## Background

Multiple weight loss interventions have been developed during the past decades. They include lifestyle and behavioral interventions (eg, diet and exercise), Anti-Obesity medications (AOMs), endoscopic interventions, and surgical procedures. Anti-Obesity medications are an effective treatment for weight loss, aiming to improve quality of life and control weight-related comorbidities. Currently, only 5 medications—orlistat, phentermine plus topiramate, naltrexone plus bupropion, liraglutide, and Semaglutide—have been approved by the US Food and Drug Administration (FDA) for long-term use in individuals with a body mass index (BMI; calculated as weight in kilograms divided by height in meters squared) of 30 or more with no weight-related comorbidities or 27 or more with weight-related comorbidities.

The incretin, glucagon-like peptide 1 (GLP-1), is a well-known incretin peptide discharged into the circulation by scattered gastrointestinal and endocrine cells. It is a gut-derived hormone that potentiates glucose-dependent insulin excretion from the pancreatic  $\beta$ -cells when blood glucose is high and contributes to glucose homeostasis. Also, GLP-1 can improve metabolic, glycemic control, and weight loss via suppression of glucagon secretion, delay in gastric clearing, gastrointestinal fat absorption, and reduced food intake. GLP-1 receptor agonists approved in the United States for treating type 2 diabetes include semaglutide, liraglutide, lixisenatide, albiglutide, and dulaglutide.

## Literature Review

Obesity is a chronic disease and global public health challenge [1-3]. Obesity can lead to insulin resistance, hypertension, and dyslipidemia [4], is associated with complications such as type 2 diabetes, cardiovascular disease, and nonalcoholic fatty liver disease [2, 5], and reduces life expectancy [6]. More recently, obesity has been linked to increased numbers of hospitalizations, the need for mechanical ventilation, and death in persons with coronavirus disease 2019 (Covid-19) [7, 8].

Although lifestyle intervention (diet and exercise) represents the cornerstone of weight management [1, 2], sustaining weight loss over the long term is challenging [9]. Clinical guidelines suggest adjunctive pharmacotherapy, particularly for adults with a body-mass index (BMI, the weight in kilograms divided by the square of the height in meters) of 30 or greater, or 27 or greater in persons with coexisting conditions [1, 2, 10]. However, the use of available medications remains limited by modest efficacy, safety concerns, and cost [3].

Semaglutide is a glucagon-like peptide-1 (GLP-1) analogue that is approved, at doses up to 1 mg administered subcutaneously once weekly, for the treatment of type 2 diabetes in adults and for reducing the risk of cardiovascular events in persons with type 2 diabetes and cardiovascular disease [11]. Semaglutide induced weight loss in persons with type 2 diabetes and in adults with obesity who were participants in a phase 2 trial [12-14], findings that supported further investigation. The global phase 3 Semaglutide Treatment Effect in People with Obesity (STEP) program aims to evaluate the efficacy and safety of semaglutide administered subcutaneously at a dose of 2.4 mg once weekly in persons with overweight or obesity, with or without weight-related complications [15].

This 68-week trial evaluated the efficacy and safety of semaglutide as compared with placebo as an adjunct to lifestyle intervention for reducing body weight and meeting other related end points in adults with overweight or obesity and without diabetes.

## Case Presentation

We are presenting one of my lovely patients, a 29-year-old pleasant female, who is has been struggling to lose her first pregnancy weight.

She was pregnant 2 years ago, and this pregnancy went uneventfully well.

She enjoyed her pregnancy, with an acceptance to her gradual weight gain in it as it was within the normal weight gain with pregnancy.

This pregnancy ended at term with a normal vaginal delivery and a beautiful baby boy, who was healthy too.

She was enjoying the postpartum period snuggling her baby boy and breastfeeding him, until the conflicts between her and her husband started to escalate. This resulted in extreme tense and stress in her mental and physical health.

Shortly after, they decided to get separated. Although it was a good decision for their relationship and for her mental health, it added a huge amount of stress on her as a single parent.

She decided to move closer to her mother. She also needed to apply for a job and to get her baby boy registered in a daycare. She was very overwhelmed, as she was grieving her previous relationship too.

She was very anxious, depressed, stressed and overwhelmed, so she decided to go to a walk-in clinic to seek medical advice.

She was diagnosed with acute reaction to stress on the top of generalized anxiety disorder, a major depressive disease and ADHD. And she was prescribed an antidepressant, SSRI, and a CNS-stimulant for ADHD.

She started taking the medications, with gradual minimal help.

She decided to seek psychotherapy too, that she found very beneficial for her as she took as an exploratory journey to increase her self-awareness, repairing her self-confidence and grasping new tools to help her coping with her new life changes and most importantly for her is to help her how to ground and relax so she can provide the best care she can to her little boy.

She was trying to build a healthy support system for her and for her little boy, and with seeing a different family physician every time she needs to ask a question or refilling her meds, she feels that this is not the ideal situation for her physical and mental health, so she decided to look for a family physician to help her through this new challenging chapter of her life.

She came to us as a meet and greet and we saw how resilient she is and she wants to be, she was a young passionate lady who was eager to work on her self-development project to get the best self that she always dreamed about. She told us that mentally, she feels she is on the right track with her mother's support, psychotherapy and the medications that started to kick in effect. Despite that, she still can't feel satisfied with her mental health as her physical health is not as she wishes, particularly, her body weight and shape. She disclosed with me that she can't get back to her pre-pregnancy weight.

When we dig deeper, she has several obstacles that make her weight loss journey more challenging. One of her main challenges is meal preparation, as she is a full-time worker and a single parent, it is very challenging for her to prepare healthy meals every day.

Secondly, she could not find time to go to the gym, as she drops off her baby at the daycare and goes to work in the morning and at the end of the day, she picks him up and go home together. Her evening usually will be taking care of her infant and eating what is available that must be fast and easy to do and not necessary to be healthy, before her little boy sleeps and she finally crashes to bed, to get some sleep before he wakes up for his next feed. So, it is really challenging for her to go to gym as she can't leave him alone at home, and she can't exercise at home as she does not have energy to do so.

In addition to unhealthy fast meals and lack of exercise, she was still going through stress and anxiety in how to manage her new life, and she was feeling depressed as a new mother but also single. So, she used to get emotional eating and sugar craving with treats snacking every day, that was giving her some transient pleasure that used to fade quickly leaving her craving more and feeling guilty about gaining more weight without being able to stop that emotional eating. The increase of her body weight started to affect her physically and mentally. Physically, by getting tired easily which she can't afford with her busy work and a single mother who is expected from herself to give to her work and to her baby at home. Also, she notices more frequent tension headaches that affect her daily performance.

Mentally, her weight had an impact on her self-esteem, self-confidence, and self-image acceptance that was worsening her anxiety and depression, and causing more distraction at work that worsening her ADHD symptoms and affecting again her daily work performance and social interaction at work for any teamwork tasks that she used to avoid as much as she can.

She came to us asking for a new family physician who can handle her physical and mental health to her best interest, which was exactly meeting our style of family medicine practice. We expressed our willingness to be part of her support system, and she agreed to that too.

## **Method and Intervention**

### ***Ethical clearance***

For ethical and confidentiality purposes name of the subject who participated in this study was not included in the data collection instruments.

### ***Data collection***

We abstracted demographic, anthropometric, and laboratory data within 30 days before or after 3 and 6 months. We collected patient weights in kilograms that were obtained either using a calibrated scale during office visits or reported by the patients during virtual visits and clinical communications with the physician.

On her first appointment with us in Calgary-Alberta, Canada, we suggested starting with a baseline physical examination, laboratory work and to go from there. She agreed to go for that.

After discussing the results of the physical examinations and lab work, we agreed to build a collaborative integrative teamwork.

So, we suggested a dietitian, which she was happy with that, as it is one of her main challenges in managing her body weight. She needed help with meal preparation and to get nutritional awareness about healthy diet that she can follow and easy to apply for her.

Regarding exercise, we discussed suitable alternatives like home exercise and starting very mild and gradual. And she liked the idea, and she was willing to try.

Regarding the medications, she was already on medications for her mental health:

1. SSRI, Escitalopram 10mg PO, daily.
2. Bupropion 150 mg PO, daily.
3. Lisdexamfetamine 20 mg PO, daily.

The medications were giving her some help but not enough to control her anxiety, depression, and lack of attention that she was having. This is because the underlying root causes of her mental health are not resolved, including the recent stressful changes in her life and her body weight that she was not happy with and gave her significant frustration and lack of self-esteem.

We conducted PHQ9 and GAD7 questionnaires and accordingly, we communicated with her psychologist to customize her therapy to manage her needs. We suggested not to rush to increase the medications at that time as it will be more beneficial to manage the root causes rather than mask it with higher doses of the medications that can give her more side effects. and there were not red flags for us to increase the doses as there were no homicidal/suicidal thoughts, she was still able to perform her daily activities as much as possible. She was happy with that as she had some side effects from the medications already.

For example, she tried a higher dose of Lisdexamfetamine before that gave her insomnia, and higher dose of SSRI that gave her some nausea.

She asked me about the injectable medications that can help her appetite, as her mother tried one of them and it worked for her, and she lost 40 pounds in 6 months.

We had a long discussion on that, and I explored with her the mechanism of action of Semaglutide, and is that it suppresses the appetite center, by delaying the gastric emptying.

We also discussed the efficacy of it, and it can help her to get rid of the extra weight, but also the beneficial effect on her blood glucose levels that can prevent insulin resistance and eventually prevents type II DM.

We also explored the side effects of Semaglutide like nausea, vomiting, prolonged bile stasis and risk of gall stones, cholecystitis and pancreatitis as well. And how to avoid these side effects by increasing hydration and healthy meals with low carbohydrate and unhealthy fat intake.

For the doses, I suggested starting with low dose, which is 0.25 mg subcutaneously weekly. And to increase it to 0.5 mg from week 2-3 depends on her body response of appetite suppression and side effects. We discussed that we could go up to 1.0 mg weekly if needed.



## Results

### *Diet*

From September 2022 until March 2023, the participant started seeing a dietitian to manage her meals, so she started to cook for herself on the weekends healthy meals and to put them on containers for work and to be ready for heating once she is home after work, avoiding ordering fast food.

She also started to increase her water intake from 1-2 cups/day to 8 cups/day, that she notices a magnificent improvement in her mood, skin health and her bowel movements regulations.

### *Exercise*

She started doing mild exercise at home after she was home. That improves her muscle tone and power as well as boosting her mood and helping her mental health.

### ***Semaglutide***

She started Sameglutide 0.25 ml weekly, and she experienced some nausea that was transient and manageable with more water and meals.

From week 4, she increased the dose to 0.5 ml that she found helping more with appetite suppression.

She tried 0.75ml in week 6, but it gave her severe nausea and vomiting, so she went back to 0.5 ml weekly that seems to help.

Regarding the body weight, she gained 20 pounds from her pregnancy that she could not lose for more than 18 months.

In September 2022, her body weight was 73.2 kilograms, and her height was 158 centimeters, and her body mass index was 29.3 at that time.

In March 2023, her body weight was 61.2 kilograms, and her body mass index was 23.9. which means she lost 16.3% of her body weight in 6 months period. And she lost 5.4 of her Body Mass Index, with this magnificent decline in her weight and body mass index putting her in the healthy normal weight category instead of Obesity category.

### ***Laboratory results***

Regarding her laboratory results, we noticed significant changes. In September 2022, her Hemoglobin A1c was 5.7% and in March 2023, it decreased to 5.4 % with 0.3% in total.

Additionally, her Triglyceride was higher than normal with 1.94 millimole/liter, and it declined to near normal with 1.75 millimole/liter in 6 months with almost 0.2 millimole/liter decline.

We also noticed a magnificent increase in her Ferritin levels, as it was 21 ug/L in September 2022, and 6 months later with a healthy diet it went up to 42 ug/L.

### ***Mental Health***

Her PHQ9 dropped from 18 to 9, with a significant 50% reduction.

Her GAD7 score dropped magnificently from 14 to 8, with 40% reduction.

Mentally, she feels much happier and calmer. She regains her self-esteem and self-confidence. She feels herself again as a social butterfly, so she started to enjoy the teamwork tasks and perform excellently on them. She is happy about the positive feedback from her supervisor and her co-workers.

She also notices a great improvement in her energy levels, as she does not struggle anymore on waking up and getting herself and her little son ready. She is happy to come home and play with her son while doing her home exercises. She is enjoying watching her son growing and reaching out to stuff on the counters that she needs to push back away from him. She is now coming to me for follow up with a beautiful big smile on her face with total acceptance to what she went through, and she is feeling proud of herself to be able to manage and cope to overcome such a tough challenge in her life with separation and being and single mother. She is now looking at herself as a single mother with pride and strength rather than overwhelming tasks.

Thanks to the customized psychotherapy that helped her to manage her anxiety and to find her a healthy release of her emotions with mindfulness practices and exercise rather than emotional eating.

And big thanks to Semaglutide that helped her with suppressing her appetite, decreasing her sugar craving, and managing her meals portions.

## Conclusion

We found that an adult with obesity (or overweight) and without diabetes had a weight loss of 16.3% from the baseline with Semaglutide as an adjunct to lifestyle intervention.

According to previous research, that showed the correlation between overweight and predisposition to metabolic syndrome and the association with insulin resistance and type II diabetes and other health-related problems. We found significant improvements in our participant's physical and mental health.

We recommend the use of Semaglutide as an adjunct to lifestyle intervention to help manage overweight and obesity.

We recommend that lifestyle intervention is still the key for achieving healthier weight.

We do see how the cost of the medication can be an obstacle to accessing it, so we do recommend getting it under some sort of health coverage, to make it more affordable to the population in need.

We do recommend more studies to support the use of Semaglutide and to explore more long-term side effects.

We do strongly recommend increasing the awareness and to work more in Obesity psychiatry, by providing more free courses for the physicians, nurses, dietitians and other health professionals to increase their awareness of the mental background of the patients with obesity.

Additionally, providing free resources to the general population to increase the awareness of the obesity consequences on mental and physical health.

This is mainly to work on the stigma behind being overweight or obese, that will eventually help and encourage the general population to access and seek health and medical support. And eventually this will help to treat and decrease the prevalence of obesity and its subsequent comorbidities.

In our opinion Semaglutide is clinically effective for weight loss for people with overweight or obesity.

## Disclosure

The authors whose names are listed immediately below certify that they have NO affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

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