

Review Article

Semaglutide and the skin: A brief review of dermatologic implications

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ABSTRACT

Semaglutide, a glucagon-like peptide-1 (GLP-1) receptor agonist, is widely used for the management of Type II diabetes mellitus. However, its increasing off-label use for rapid weight loss has brought attention to its unintended effects on facial esthetics and skin health. One of the most prominent consequences is “semaglutide face,” characterized by facial hollowing, loss of subcutaneous fat, skin sagging, and premature aging due to fat redistribution, collagen depletion, and muscle loss. This article explores the mechanisms by which semaglutide affects the skin and overall appearance, highlighting the accelerated aging process caused by reduced elastin, collagen breakdown, and structural changes in facial anatomy. The clinical presentation of semaglutide-induced facial changes and the available treatment modalities – ranging from dermal fillers, platelet-rich plasma, and radiofrequency microneedling to surgical interventions such as facelifts and fat grafting – are discussed. While semaglutide offers significant metabolic benefits, its esthetic implications necessitate careful patient counseling and treatment planning. Understanding the dermatological effects of GLP-1 agonists is crucial for physicians and dermatologists to provide appropriate interventions and mitigate unwanted facial changes in patients undergoing semaglutide therapy.

Keywords: Diabetes, Glucagon-like peptide-1, Ozempic, Semaglutide, Weight loss

INTRODUCTION

Semaglutide, a form of semaglutide, is a glucagon-like peptide-1 (GLP-1) receptor agonist primarily used to treat Type II diabetes mellitus. However, over time, it has gained significant attention for its rapid weight loss effects, which have led to a distinctive facial appearance popularly termed “semaglutide face.”^[1]

Semaglutide is associated with various skin-related side effects, including dysesthesia, hyperesthesia, neuralgia, paresthesia, sensitive skin, and a burning sensation upon oral administration.

Common semaglutide-based medications include Semaglutide, Rybelsus, and Wegovy. While Rybelsus is prescribed for Type II diabetes mellitus, Wegovy is primarily used for weight loss and cardiovascular conditions.^[2]

Although semaglutide is officially approved for diabetes management, it has gained widespread popularity on social media due to its weight loss effects. By lowering blood sugar levels, it also induces weight loss in diabetic patients. This often results in a noticeable loss of facial volume

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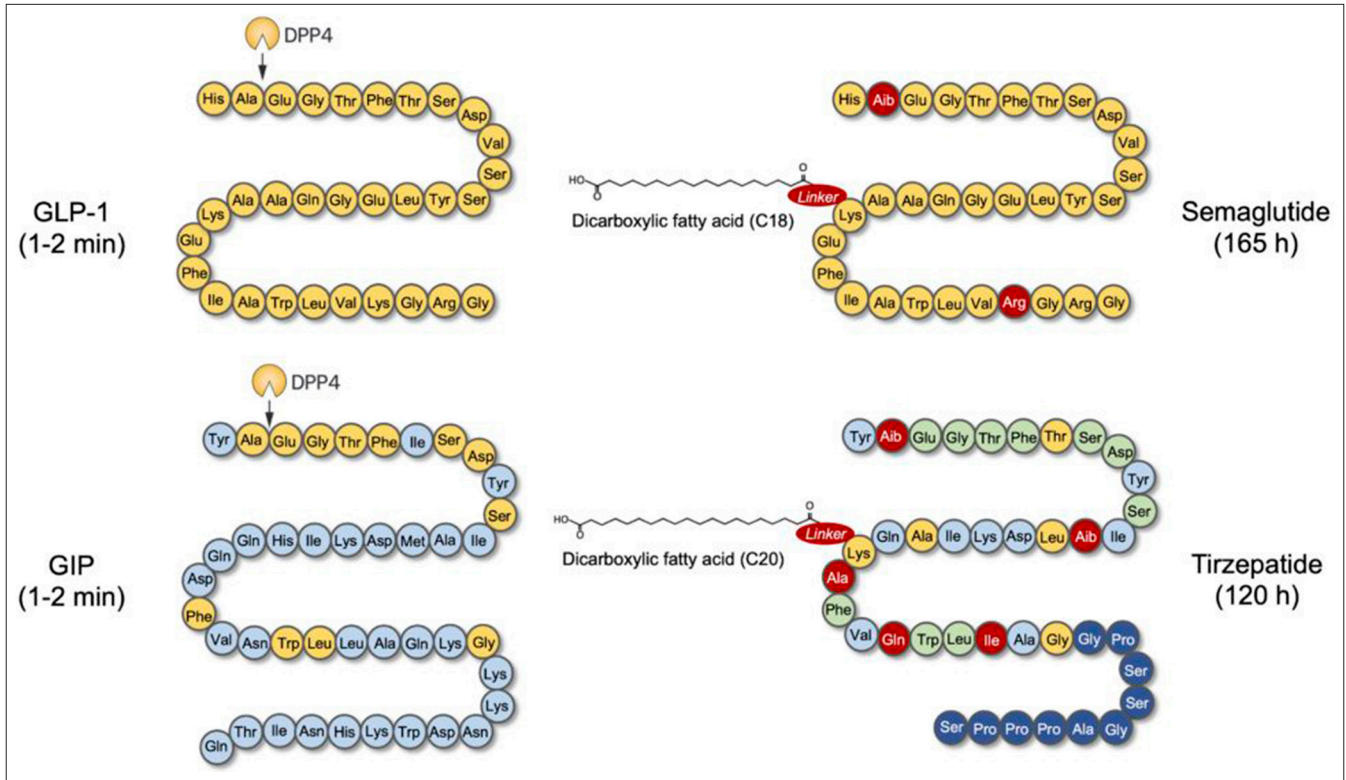


Figure 1: Structure of semaglutide. GLP-1: Glucagon-like peptide-1, GIP: Gastric inhibitory polypeptide, DPP4: Dipeptidyl peptidase-4.

and gauntness, commonly referred to as “semaglutide face.” This occurs due to subcutaneous fat loss, giving the face a “sunken-in” appearance.^[3]

One reason semaglutide is widely used is its 94% structural homology with human GLP-1. It is administered either as an oral tablet or a subcutaneous injection, typically given once weekly, though in severe cases, daily dosing may be required. In 2021, it received approval for chronic weight management due to its significant role in rapid weight reduction.^[1,4]

MECHANISM OF ACTION

Semaglutide is a GLP-1 receptor agonist [Figure 1] that enhances insulin secretion while reducing glucagon release. It binds to GLP-1 receptors located in the gastrointestinal tract, pancreas, and brain, with its primary action occurring in the pancreas.

When blood glucose levels rise, semaglutide stimulates glucose-dependent insulin secretion from the β-cells of the pancreas. This process increases insulin release while simultaneously suppressing glucagon secretion, thereby maintaining normal blood glucose levels. Notably, semaglutide lowers glucose levels in hyperglycemia without causing hypoglycemia, making it a preferred treatment for diabetes mellitus^[1] [Figure 2].

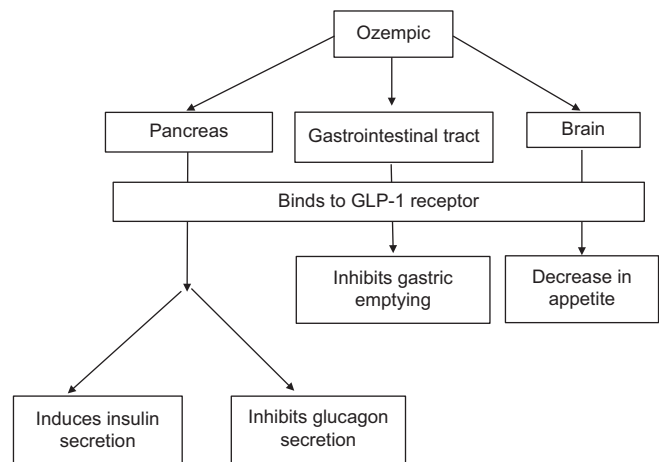


Figure 2: Flowchart of mechanism of action of ozempic.

Beyond its effects on glucose regulation, semaglutide also acts on GLP-1 receptors in the hypothalamus, leading to appetite suppression and reduced food cravings. This results in prolonged intervals between meals, decreased calorie intake, and delayed gastric emptying, ultimately contributing to significant weight loss – one of the drug’s most prominent side effects.

Due to this mechanism, semaglutide not only helps maintain blood glucose levels but also induces rapid weight loss,

particularly noticeable in the face, a phenomenon commonly referred to as “semaglutide face.”^[2]

FEATURES OF SEMAGLUTIDE FACE

Semaglutide leads to rapid weight loss, which contributes to a distinct facial appearance known as “semaglutide face.” This condition is characterized by temporal hollowing, earlobe thinning, facial narrowing, visible platysmal bands, prominent deep wrinkling, deepening of facial folds, and skin sagging, which results in marionette lines. In addition, it causes deepening and thinning of the nasolabial folds along with jowling, giving the face a more aged and gaunt appearance.^[5]

The most noticeably affected areas include the cheeks, temples, neck, and periorbital region, where the loss of subcutaneous fat becomes particularly evident. Due to the rapid reduction in facial volume, semaglutide may also accelerate the aging process, altering the size, shape, and proportion of features such as the lips, chin, and cheeks.^[6,7]

HOW SEMAGLUTIDE AFFECTS THE EVERYDAY LIFE

Semaglutide-induced rapid weight loss can significantly impact daily life by accelerating the aging process. One of its primary effects is on fat, fibers, and muscle mass, which naturally decline with age. However, in individuals taking semaglutide, these changes occur at a much faster and more pronounced rate.^[8]

Fat redistribution due to semaglutide can lead to a hollowed-out or sagging appearance, particularly in the cheeks, temples, and around the eyes, while excess fat may accumulate in areas such as the jowls and under the chin. This redistribution contributes to the characteristic “semaglutide face.”^[2,7]

In addition, elastin and collagen, the essential fibers responsible for skin elasticity and firmness, gradually decrease with age. However, semaglutide accelerates this decline, leading to faster skin sagging and wrinkling. The loss of muscle mass, including facial muscles, further contributes to a prematurely aged appearance. Studies suggest that 20–50% of the total weight loss in individuals using semaglutide is due to muscle mass reduction, which is particularly evident in those with significant initial body weight.^[9]

The combined effects of fat redistribution, fiber depletion, and muscle loss contribute to enhanced signs of aging, making individuals appear older than their actual age. These changes can impact self-esteem, social interactions, and overall quality of life, particularly for those who experience dramatic facial and body transformations after using semaglutide.^[10]

MANAGEMENT OF SEMAGLUTIDE SIDE EFFECTS

Medical management

There are several approaches to managing semaglutide-induced weight loss. One of the primary steps in treatment is discontinuing semaglutide, allowing for the regain of lost body weight, a process known as “semaglutide rebound.” This term refers to weight regain after stopping semaglutide treatment.

However, many individuals are reluctant to regain weight after experiencing significant weight loss, making discontinuation an unfavorable option. A study conducted on 327 non-diabetic individuals who received a once-weekly 2.4 mg dose of semaglutide found that participants regained two-thirds of their lost weight within 1 year of stopping the medication. This indicates that while discontinuing semaglutide can lead to weight regain, the process is not always complete or predictable.^[11]

The advantages of stopping semaglutide include preventing further volume loss and eliminating ongoing medication costs. However, the disadvantages include the possibility of regaining lost weight, incomplete reversal of aesthetic changes, and, in cases requiring corrective procedures, high costs, invasiveness, and longer recovery times.^[12]

DERMATOLOGICAL INTERVENTION

Dermal fillers

As the name suggests, dermal fillers are injectable treatments used to restore lost volume and reduce wrinkles. These fillers work through two primary mechanisms: Physically filling the treated area and stimulating collagen synthesis to enhance skin structure and elasticity.

Common types of dermal fillers include hyaluronic acid-based fillers, calcium hydroxylapatite, poly-L-lactic acid, and polymethylmethacrylate. These fillers improve facial fullness and help reduce the appearance of hollowing, particularly in areas affected by rapid weight loss. They also stimulate type I collagen production and elastic fiber synthesis through the transforming growth factor-beta/Smad pathway, further enhancing skin firmness and elasticity.

The advantages of dermal fillers include their quick and minimally invasive nature, immediate results with little to no downtime, and the ability to be customized for specific areas of volume loss. However, the disadvantages include the need for repeat treatments, as fillers are temporary, and potential side effects such as bruising, swelling, infection, allergic reactions, necrosis, or migration of the filler.^[13-15]

Platelet-rich plasma (PRP) injections

PRP therapy is a regenerative treatment that utilizes a patient's own blood-derived growth factors to rejuvenate the skin, reduce wrinkles, and improve skin texture. It is also increasingly used for addressing semaglutide face, helping to restore lost volume and enhance skin elasticity.^[16]

The procedure works by stimulating fibroblast proliferation, which in turn boosts type I collagen synthesis, accelerates the healing process, and reduces recovery time. Since PRP is derived from the patient's own blood, it significantly lowers the risk of allergic reactions or immune responses.

The advantages of PRP therapy include its natural approach, as it utilizes the patient's own cells, and its ability to stimulate collagen and elastin synthesis, promoting firmer, healthier skin. However, the drawbacks include the requirement of a blood draw, which may cause discomfort or bruising.^[16-18]

Radiofrequency microneedling (RFM)

RFM is a minimally invasive procedure that combines tiny needles with radiofrequency energy to create controlled micro-injuries in the skin. This process stimulates collagen and elastin production by heating the deeper layers of tissue, leading to improved skin texture, tone, and elasticity. It is particularly effective in tightening loose and sagging skin, making it a popular treatment for semaglutide face.^[17-19]

Results typically become noticeable after 4–6 treatment sessions.

The advantages of RFM include its minimally invasive nature, short recovery time, and its ability to enhance skin texture while tightening the face. In addition, it promotes collagen and elastin synthesis, improving overall skin firmness. However, multiple sessions are required for optimal results, and the costs can add up over time.^[20]

Energy-based devices

Energy-based skin tightening treatments utilize advanced non-invasive devices to improve skin firmness and elasticity. These treatments work by stimulating collagen and elastin fiber synthesis through direct contact with the skin, effectively addressing facial laxity and drooping seen in semaglutide face.^[21,22]

Common technologies used in these procedures include fully ablative laser resurfacing devices, parallel beam ultrasound technology, and fractional energy devices. These modalities enhance skin structure, leading to a more youthful and lifted appearance.^[23]

The advantages of energy-based treatments include their non-invasive nature, ability to improve skin texture, and their role in stimulating collagen and elastin production for

long-term skin rejuvenation. However, the disadvantages include the need for multiple sessions to achieve optimal results and the high cumulative cost of treatment.^[23,24]

Surgical treatment

In surgical treatments for semaglutide face, surgical interventions offer long-lasting and significant improvements by addressing sagging skin, volume loss, and facial contouring.^[25-27]

1. Rhytidectomy (Facelift): This surgical procedure rejuvenates the face by tightening sagging tissues, removing excess skin, and repositioning underlying muscles and fat, restoring a more youthful appearance.^[28]
2. Facelifts: A comprehensive facelift involves the repositioning of adipose tissue to correct sagging. There are various types of facelifts, including general facelifts, brow lifts, and neck lifts, each targeting specific areas of facial aging.^[29]
3. Facelift with Fat Transfer: Considered one of the most effective surgical treatments, this procedure combines a traditional facelift with fat grafting. Fat is harvested from another area of the body using liposuction and strategically injected into the face to restore lost volume and reduce wrinkles.^[30]

The advantages of surgical treatments include significant, long-lasting results and the ability to address multiple areas of the face simultaneously. However, the disadvantages include invasiveness, longer recovery times, and high costs, similar to most major surgical procedures.^[31]

CONCLUSION

The effects of semaglutide on the skin underscore the broader implications of using GLP-1 receptor agonists for rapid weight loss. The drug-induced fat redistribution, facial hollowing, and volume loss result in highly noticeable esthetic changes, often referred to as the semaglutide face. Beyond its impact on fat, semaglutide also affects collagen, elastin, and muscle mass, accelerating the aging process and contributing to premature facial aging characterized by wrinkles, sagging skin, and a gaunt appearance.

Premature aging due to semaglutide is often evident through rapid and disproportionate weight loss, particularly in the face and body composition. Managing these effects involves several corrective interventions, including discontinuation of semaglutide; non-invasive dermal treatments such as RFM, PRP, energy-based skin tightening, and dermal fillers; and surgical procedures such as rhytidectomy, facelifts, and fat grafting for long-term restoration.

While semaglutide remains a valuable medication for Type II diabetes mellitus, its off-label use for weight loss should be

approached with caution. Proper patient selection, medical supervision, and awareness of its potential esthetic and metabolic consequences are essential to ensure safe and balanced treatment outcomes.

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