Since 1987
REVIEW OF CLINICAL PHARMACOLOGY AND PHARMACOKINETICS, INTERNATIONAL EDITION |38 (Sup1): 31-35 (2024) Rcpp

Received: 18 December 2023 | **Accepted**: 22 December 2023 | **Published**: 17 February 2024

Paper presented at the **1st Conference of the Hellenic Scientific Society of Aesthetics**
2-3 December 2023 | University of West Attica, Athens, Greece

Open Access | **Review Paper**

Semaglutide (Ozempic) and obesity. A comprehensive guide for aestheticians

Vasiliki Sofia Grech[1,*], Kleomenis Lotsaris[2], Ioanna Grech[3], Vasiliki Kefala[3], Efstathios Rallis[3]

[1]Medical Doctor, Department of Care and Social Services, Healthcare Services, University of West Attica, Greece
[2]Medical Doctor, Resident Psychiatrist in Psychiatry Department of General Hospital of Athens "Evaggelismos"
[3]Department of Biomedical Sciences. School of Health and Care Sciences, University of West Attica. Campus 1. Athens, Greece

***Corresponding author**
Vasiliki Sofia Grech, MD, Thivon 250, Egaleo, GR-12244, Attica, Greece. Tel +30210-5381223.
E-mail: vgkrek@uniwa.gr

Abstract
Obesity is a complex interplay of biological, genetic, behavioural, and environmental factors. Going beyond the conventional Body Mass Index (BMI) evaluation, the complex relationship between obesity and skin diseases unveils the evolving role of aesthetics in health promotion. Adipose tissue, traditionally seen as an energy reservoir, is unveiled as a dynamic endocrine organ, playing a crucial role in the pathophysiological mechanisms of insulin resistance and metabolic syndrome. This article navigates the skin-deep impact of obesity and unravelling its influence on dermatological challenges. From disrupted epidermal barriers to diseases such as psoriasis and hidradenitis suppurativa, it further explores how licensed cosmetologists emerge as health advocates. For what is more, semaglutide, a groundbreaking GLP-1 agonist, takes the spotlight, tracing its journey from FDA approval for type 2 diabetes to its recent endorsement for obesity. The article examines its mechanism, efficacy, and unintended consequences of popularity, emphasizing the need for responsible medication use.

KEYWORDS
obesity, skin, aesthetician, semaglutide

How to cite: Grech V.S., Lotsaris K., Grech I., Kefala V., Rallis E. Semaglutide (Ozempic) and obesity. A comprehensive guide for aestheticians. *Rev. Clin. Pharmacol. Pharmacokinet. Int. Ed.* 38 (Sup1): 31-35 (2024). https://doi.org/10.61873/RJDB1796

Publisher note: PHARMAKON-Press stays neutral with regard to jurisdictional claims in published maps and institutional affiliations.

1. INTRODUCTION

In the ever-expanding landscape of health and wellness, the understanding of obesity has exceeded the conventional Body Mass Index (BMI) evaluation. The centuries-long trajectory of rising BMI, the pivotal phase of adolescent development, the revealing of adipose tissue as a dynamic endocrine organ and the inflammatory profile of obesity, are unfolding the multifaceted dimensions of this disease. In addition, the need for responsible medication use is addressing the multifaceted challenges posed by obesity.

In this context the article holds significance in the pursuit of holistic health into bridging the gap between beauty and wellness. Licensed cosmetologists foster health-related conversations and pos-

itive health changes among clients, play a vital role. This active intervention appears to be crucial at the point where beauty meets health and skincare intertwines with well-being.

2. UNDERSTANDING OBESITY BEYOND BMI

Obesity, a chronic and multifaceted disease, is often evaluated using BMI, a measure derived from weight and height. However, BMI has limitations, failing to consider factors such as fat distribution and specific biochemical influences on mortality risk. To address these shortcomings, alternative assessments, including waist circumference, waist-to-thigh ratio, skinfold measurements, and direct fat percentage evaluation via dual X-ray absorptiometry (DXA), are crucial for a more accurate understanding of central obesity [1].

Historical data reveals a continuous increase in BMI over the past three centuries. Economist R Fogel's tracking of body size from the early 1700s to nowadays highlights a steady rise in BMI. Contrary to perceiving obesity as a recent "epidemic," this historical perspective suggests that human effort to protect against famine have contributed to the longlisting trajectory of rising BMI [2].

Adolescence is a crucial phase in human's development and understanding the factors contributing to weight-related issues throughout this period is imperative. Two significant studies for Greece, the Feeding Exercise Trial in Adolescence and the Health Behaviour in School-aged Children, shed light on the intricate web of elements influencing the weight of teenagers. Both outcome at the same result showing that one quarter of the examined population are either overweight or obese. From familial dynamics to individual eating behaviours, the complex interplay of these elements necessitates a holistic approach to address adolescent obesity [3,4].

3. ADIPOSE TISSUE AS AN ENDOCRINE ORGAN

Adipose tissue, traditionally viewed as a mere energy reservoir, is now recognized as a dynamic endocrine organ. With roles extending beyond thermoregulation and energy storage, adipose tissue also secretes numerous of substances, including adipokines such as leptin and adiponectin, peptides like angiotensinogen, apelin and resistin and inflammatory cytokines including IL-6, TNF-a, visfatin, omentin and chemerin and last but not least steroid hormones. These substances tortuously contribute to the pathophysiological mechanisms underlying insulin resistance and metabolic syndrome. Leptin, a hormone primarily produced by adipose cells, takes centre stage in the regulation of appetite, energy expenditure, and glucose homeostasis. In obesity, a condition characterized by hypertrophy and hyperplasia of fat cells, leptin resistance emerges. This resistance leads to a cascade of detrimental effects, including the promotion of pro-inflammatory reactions, reversal of appetite control, increased inflammation, and a higher likelihood of cardiac events. In contrast, adiponectin, known for its anti-atherosclerotic, anti-inflammatory and anti-diabetic properties, appears to decrease during obesity, contributing to disturbances observed in individuals with excess body weight. The implications of obesity extend far beyond beauty concerns, manifesting in a spectrum of health issues. Cardiovascular diseases, respiratory diseases, type 2 diabetes, non-alcoholic fatty liver disease, metabolic syndrome, musculoskeletal diseases, psychiatric disorders, central and peripheral nervous system complications, malignancies, infertility, and skin diseases are among the plethora of conditions associated with obesity [5,6].

4. THE SKIN-DEEP IMPACT OF OBESITY

Obesity triggers a cascade of disruptions in the delicate balance of skin components, leading to a spectrum of dermatological challenges. The epidermal barrier, essential for moisture retention, succumbs to increased water loss and dryness. Simultaneously, collagen, a structural protein crucial for skin integrity, undergoes changes, fostering dysfunction in healing processes and elevating the risk of ulcers. The sebaceous glands, influenced by heightened levels of androgens, insulin, and growth hormone in obesity, overproduce sebum. This excess sebum exacerbates conditions like acne, contributing to a more challenging clinical picture. Sweat glands, particularly in skin folds with thicker layers of subcutaneous fat, face dysfunction in sweat evaporation and local pH imbalance, creating a breeding ground for micro-inflammations and the growth of dermatophytes or bacteria, often even resulting in the notorious "bromhidrosis." Obesity's impact extends to the circulatory system, with microcirculation dysfunction leading to microangiopathy and hypertension. Vascular hypertension and valvular insufficiency, often intensified by increased intra-abdominal pressure, contribute to varicose eczema and ulcers. Lymph stasis further adds to the complexity, leading to lymphedema, reduced tissue oxygenation, and heightened vulnerability to local infections [7].

The intertwining relationship between obesity and specific skin diseases is evident in conditions

like psoriasis and hidradenitis suppurativa. At 2020, a research made by Egeberg et al, highlights the correlation between obesity and elevated levels of IL-23, Th-17 and leptin, pivotal molecules in the pathophysiology of psoriasis and cardiometabolic comorbidities [8]. Epidemiological studies as well reveal a bidirectional relationship between obesity and psoriasis, where increased BMI amplifies the risk of psoriasis and vice versa, while falling its systemic treatment effectiveness [9].

Hidradenitis suppurativa, affecting approximately 1% of population in EU, initiates as an infection of sweat glands, leading to painful nodules, abscesses, and fistulas. The mechanical friction in large skin folds, prevalent in obesity is contributing to its formation and the quality of life is significantly impacted with chronic inflammation occasionally progressing to malignancy. In a study of 302 hidradenitis patients, those with a BMI ≥30 kg/m² showed a prevalence of 21%, emphasizing the importance of weight management in improving treatment outcomes, including remission [10].

For what is more, skin disorders like lipodermatosclerosis, palmoplantar keratoderma, intertrigo, acanthosis nigricans, cellulite, erysipelas, onychomycosis, hyperandrogenism with or without the presence of hirsutism and less frequently necrotizing fasciitis and gas gangrene are commonly seen in obese individuals [7]. It becomes evident that weight management is not only crucial for internal health but also for maintaining the integrity and well-being of the skin. A holistic approach to health that addresses both internal and external manifestations is imperative in tackling the multifaceted challenges posed by obesity.

5. BRIDGING BEAUTY AND WELLNESS: THE VITAL ROLE OF AESTHETICIANS IN HEALTH PROMOTION

In the realm of aesthetics, where beauty is often the primary focus, a silent yet powerful transformation is occurring—one that transcends traditional cosmetic concerns. This article explores the evolving role of licensed cosmetologists as health advocates, shedding light on their ability to impact not only physical appearance but also the overall well-being of their clients. Health, as defined by the World Health Organization (WHO), is intricately woven into the fabric of daily life—where learning, working, playing, and loving converge. In this context the social ecological framework (SEF) is considered as a useful heuristic approach that posits that individual health behaviour is influenced at multiple levels including intrapersonal, interpersonal, organizational, community, and policy standards [11].

Numerous studies since 1979 highlight beauty salons as an environment ripe for the exchange of social support, advice, and empathy, particularly among women. An intriguing admission emerges as licensed cosmetologists actively engage in health-related conversations during their interactions with clients. These professionals, often seen as confidants, play a pivotal role in transmitting health promotion messages. Empathy, evaluation, and advice become tools through which aestheticians foster a unique bond with their clients [12]. Pioneering initiatives, such as the 2005 seven-week pilot intervention in North Carolina involving trained cosmetologists, showcase the impact of these professionals on client well-being. An overwhelming 86% of customers actively discussed health concerns with their cosmetologists, leading to a substantial 55% making positive health changes over the subsequent 12 months [13]. The effectiveness of licensed cosmetologists as health messengers is underscored by the wealth of international literature. Among 110 articles aesthetics institutes are emerging as shelters for wellness, where a general audience perceives the space as a relaxation area. This environment fosters trust and opens avenues for disseminating health-related knowledge, breaking taboos, and initiating crucial health dialogues. The unique nature of the relationship between cosmetologists and clients is evident in the statistics. Most clients tend to return to the same cosmetologist over several years, spending substantial periods—ranging from 1.5 to 3 hours—with them. This continuity enables cosmetologists to not only understand the cosmetic preferences of their clients but also to delve into their broader health concerns [14].

In light of these insights, cosmetologists emerge as more than just beauty professionals—they are natural assistants and trusted community members. Beyond enhancing physical appearance, they are becoming catalysts for health improvement and promotion within their workplaces and local environments. The cosmetologist, it seems, is poised to be the optimal promoter of holistic health, bridging the realms of beauty and wellness [14].

6. SEMAGLUTIDE: A GROUNDBREAKING GLP-1 AGONIST

In the ever-evolving landscape of medical advancements, semaglutide (ozempic), stands as a beacon of progress. Originally FDA-approved in 1997 for the management of type 2 diabetes, its recent approval in 2021 for obesity has sparked a

fervour for new slimming solutions, marking a significant leap in the pharmaceutical pursuit of holistic health. A testament to semaglutide's impact is the staggering 152% increase in prescriptions in the US in 2023 alone. However, this surge, while indicative of its success, has unintended consequences, resulting in a 72% greater market increase than initially anticipated. This popularity, while affirming its efficacy, raises concerns about the overconsumption of these drugs, potentially limiting access for those who need them the most [15]. At the heart of semaglutide's prowess lies the mechanism of GLP-1 (Glucagon-Like Peptide-1) agonists. Incretins like GLP-1 and GIP (Gastric Inhibitory Polypeptide), secreted by the intestinal mucosa, induce insulin secretion, effectively reducing glucose levels—a phenomenon first described in 1929 as the "Incretin phenomenon." Unlike the naturally produced GLP-1 that is broken down by DPP-4 (dipeptidylpeptidase 4), its counterpart GLP-1 agonist is more resilient to DPP-4 and reproduces a longer lasting action. The multifaceted properties of GLP-1, including appetite suppression, delayed gastric discharge, reduced blood glucose levels, and enhanced insulin secretion, collectively contribute to long-term results. Studies show a reduction in HbA1C% and sustained lower body weight, making them promising tools in the management of diabetes type 2 and obesity [16]. While the benefits of GLP-1 agonists are notable, they come with their share of side effects. Dose-dependent reactions such as nausea, vomiting, dizziness, and diarrhoea can be substantial. Severe cases might lead to a reduction in volume and acute kidney damage and allergic reactions ranging from moderate to severe, underlining the importance of careful administration [17,18].

Semaglutide's efficacy in treating obesity is underscored by extensive studies. At 2021 Wilding et al., completed a double-blind, placebo-controlled study involving1961 non-diabetic participants with a BMI ≥ 30, resulting in clinical relevant wight loss with weekly injections of 2.4mg of semaglutide, establishing it appropriate for weight loss management in combination with lifestyle changes [19]. However, it's crucial to note that the favourable effects on weight may be transient, with bibliographic evidence suggesting weight regain after discontinuation [20].

Looking ahead, the pharmaceutical landscape in obesity treatment is dynamic. Current options for pharmaceutical weight loss in Greece include only orlistat, naltrexone/bupropion, and liraglutide 3 mg. Semaglutide is not an option for weight loss at the moment, since all the available preparations are intended for the treatment of type 2 diabetes and dose up to 1mg [20]. The next big frontier is tirzepatide, a GIP/GLP-1-agonist and is poised for exploration. The 2022 international, double-blind study of 2539 obese, non-diabetic participants aim to evaluate the efficacy of tirzepatide at different doses. All three doses of once a week subcutaneously led to clinically meaningful and sustained weight reduction. Albeit with potential side effects such as nausea, diarrhoea, and constipation [21].

Semaglutide's journey from a diabetes management drug to an obesity treatment heralds a new era in pharmaceutical solutions. As research propels us towards novel approaches, it is imperative to strike a balance between the benefits of these advancements and the responsible use of these medications, ensuring equitable access to transformative therapies for all in need.

7. CONCLUSION

In the intricate web of health complexities, the skin emerges as a silent storyteller, revealing tales of distress through conditions like psoriasis, hidradenitis suppurativa and obesity. These manifestations not only impose a burden on the individual but also intertwine with therapeutic responses. Among these complexities, a figure often underestimated in the healthcare narrative, emerges—the aesthetician. Positioned catalytically, the aesthetician assumes the role of an optimal health promoter. Beyond the territories of aesthetic enhancements, they become conduits of health promotion, engaging in discussions that exceed the traditional boundaries of beauty.

On top of that, pharmaceutical advancements and challenges persist in the fight against obesity. Yet, the reckless use of anti-diabetic drugs for weight loss management burdens diabetic patients, as in Greece where the current doses of semaglutide are indicated only for type 2 diabetes. However, a glimmer of hope shines on the horizon. In this dynamic landscape, where beauty meets health, and skincare intertwines with well-being, the journey continues. The aesthetician, once confined to the realms of aesthetics now evolves into a holistic health advocate.

CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

REFERENCES

1. Perdomo CM, Cohen RV, Sumithran P, Clement K, Fruhbeck G. Contemporary medical, device, and surgical therapies for obesity in adults. *Lancet*.;401(10382):1116-30 (2023). **http://dx.doi.org/10.1016/s0140-6736(22)02403-5**

2. Caballero B. Humans against Obesity: Who Will Win? *Adv Nutr*.;10(suppl_1): S4-S9 (2019).
http://dx.doi.org/10.1093/advances/nmy055

3. Patsopoulou A, Tsimtsiou Z, Katsioulis A, Rachiotis G, Malissiova E, Hadjichristodoulou C. Prevalence and Risk Factors of Overweight and Obesity among Adolescents and Their Parents in Central Greece (FETA Project). *Int J Environ Res Public Health.*;13(1):83. (2015).
http://dx.doi.org/10.3390/ijerph13010083

4. Makri R, Katsoulis M, Fotiou A, Kanavou E, Stavrou M, Richardson C, et al. Prevalence of Overweight and Obesity and Associated Diet-Related Behaviours and Habits in a Representative Sample of Adolescents in Greece. Children (Basel).;9(1) (2022).
http://dx.doi.org/10.3390/children9010119

5. Fahed G, Aoun L, Bou Zerdan M, Allam S, Bou Zerdan M, Bouferraa Y, et al. Metabolic Syndrome: Updates on Pathophysiology and Management in 2021. *Int J Mol Sc*i. 23(2). (2022). **http://dx.doi.org/10.3390/ijms23020786**

6.Jin X, Qiu T, Li L, Yu R, Chen X, Li C, et al. Pathophysiology of obesity and its associated diseases. *Acta Pharm Sin B*.13(6):2403-24. (2023).
http://dx.doi.org/10.1016/j.apsb.2023.01.012

7. Hirt PA, Castillo DE, Yosipovitch G, Keri JE. Skin changes in the obese patient. *J Am Acad Dermatol*. 81(5):1037-57. (2019).
http://dx.doi.org/10.1016/j.jaad.2018.12.070

8. Egeberg A, Gisondi P, Carrascosa JM, Warren RB, Mrowietz U. The role of the interleukin-23/Th17 pathway in cardiometabolic comorbidity associated with psoriasis. *J Eur Acad Dermatol Venereol*.;34(8):1695-706. (2020).
http://dx.doi.org/10.1111/jdv.16273

9. Kong Y, Zhang S, Wu R, Su X, Peng D, Zhao M, et al. New insights into different adipokines in linking the pathophysiology of obesity and psoriasis. *Lipids Health Dis*.;18(1):171. (2019).
http://dx.doi.org/10.1186/s12944-019-1115-3

10. Van Straalen KR, Prens EP, Gudjonsson JE. Insights into hidradenitis suppurativa. *J Allergy Clin Immunol.*;149(4):1150-61 (2022).
http://dx.doi.org/10.1016/j.jaci.2022.02.003

11. Linnan LA, Ferguson YO. Beauty salons: a promising health promotion setting for reaching and promoting health among African American women. *Health Educ Behav.;*34(3):517-30. (2007).
http://dx.doi.org/10.1177/1090198106295531

12. Solomon FM, Linnan LA, Wasilewski Y, Lee AM, Katz ML, Yang J. Observational study in ten beauty salons: results informing development of the North Carolina BEAUTY and Health Project. *Health Educ Behav.*;31(6):790-807. (2004).
http://dx.doi.org/10.1177/1090198104264176

13. Linnan LA, Ferguson YO, Wasilewski Y, Lee AM, Yang J, Solomon F, et al. Using community-based participatory research methods to reach women with health messages: results from the North Carolina BEAUTY and Health Pilot Project. *Health Promot Pract.*;6(2):164-73 (2005).
http://dx.doi.org/10.1177/1524839903259497

14. Michalak M. The role of a cosmetologist in the area of health promotion and health education: A systematic review. *Health Promot Perspect.;*10(4):338-48. (2020).
http://dx.doi.org/10.34172/hpp.2020.52

15. Han SH, Safeek R, Ockerman K, Trieu N, Mars P, Klenke A, et al. Public Interest in the Off-Label Use of Glucagon-Like Peptide 1 Agonists (Ozempic) for Cosmetic Weight Loss: A Google Trends Analysis. *Aesthet Surg J*. (2023).
http://dx.doi.org/10.1093/asj/sjad211

16. Wojtara M, Mazumder A, Syeda Y, Mozgala N. Glucagon-Like Peptide-1 Receptor Agonists for Chronic Weight Management. *Adv Med*. 2023:9946924 (2023).
http://dx.doi.org/10.1155/2023/9946924

17. Collins L, Costello RA. Glucagon-Like Peptide-1 Receptor Agonists. *StatPearls. Treasure Island* (FL) (2023).

18. Μουσλεχ Ζ. "Ο ρόλος των ινκρετινών, των αναλόγων και των αναστολέων της διλεπτυλ-πεπτιδάσης 4 στην παθοφυσιολογία και τη θεραπευτική αντιμετώπιση του σακχαρώδους διαβήτη τύπου 2". *Ελληνικά Διαβητολογικά Χρονικά*;22 (1):25-38. (2009).
http://dx.doi.org/10.12681/eadd/51462

19. Wilding JPH, Batterham RL, Calanna S, Davies M, Van Gaal LF, Lingvay I, et al. Once-Weekly Semaglutide in Adults with Overweight or Obesity. *N Engl J Med*.;384(11):989-1002 (2021).
http://dx.doi.org/10.1056/nejmoa2032183

20. Εταιρεία ΕΔ. «Κατευθυντήριες Οδηγίες για τον Σακχαρώδη Διαβήτη». In: *Εταιρεία ΕΔ, editor. Φαρμακευτική αντιμετώπιση της παχυσαρκίας. Αθήνα*. p. 145. (2023).

21. Jastreboff AM, Aronne LJ, Ahmad NN, Wharton S, Connery L, Alves B, et al. Tirzepatide Once Weekly for the Treatment of Obesity. *N Engl J Med*. 387(3):205-16. (2022). **http://dx.doi.org/10.1056/nejmoa2206038**