VIA MEDICA

LETTER TO THE EDITOR

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Semaglutide as a chance for obesity treatment

To the Editor

Driven by the recently reported shortages of semaglutide, both I and my colleagues sought to introduce physicians to the current state of epidemiology, associated risks, and treatment strategies related to this morbidity. Moreover, we included a summary of the latest trials demonstrating its efficacy.

The prevalence of obesity has experienced a significant surge in recent decades, reaching epidemic proportions. In 2015, it was estimated that nearly 604 million adults and 108 million children were affected by obesity. The prevalence of obesity has more than doubled in over 70 countries since 1980, and this upward trend is evident across the globe [1]. Furthermore, approximately 2 billion adults are estimated to be overweight, thus being at risk of becoming obese [2]. Obesity has been linked to a multitude of coexisting disease entities, which have a major influence on mortality rates and overall quality of life. These conditions include cardiovascular disease, non-alcoholic steatohepatitis, diabetes, chronic kidney disease, and various forms of cancer [1, 3]. It is worth noting that individuals between the ages of 20 and 29 who are overweight are expected to experience a reduction in life expectancy by approximately 3.3 years, whereas those classified as obese or severely obese may face a loss of lifespan ranging from 5.6 to 10.3 years [4].

The fundamentals of obesity treatment have always been the modification of lifestyle, employment of a normocaloric or hypocaloric diet, increasing physical activity, and, in some instances, cognitive behavioural therapy [5]. Physical exercise confers advantages in the regulation of glucose levels and has been proven to be beneficial for the prophylaxis of metabolic disorders, including obesity and diabetes [6]. Research indicates that exercise leads to improvements in insulin resistance and facilitates glucose uptake in muscles by upregulating the expression of GLUT4 [6]. Furthermore, during sports training, skeletal muscles not only rely on glucose as the mere energy source, but they also utilise lipids, thereby enhancing the consumption of free fatty acids [7]. However, there are also several other available therapeutic approaches, which can be classified as surgical and pharmacological. The former method, also called bariatric surgery, can be applied in patients who fail to achieve the treatment goals with lifestyle modification and have a BMI $\geq$ 30 kg/m^2 regardless of obesity-related comorbidities, and in patients with a BMI $\geq$ 27 kg/m^2 with coexisting obesity-related diseases. Despite its effectiveness, bariatric surgery is often extensive, consequently carrying a major risk for the patient's health and safety, and sometimes it cannot be taken as viability [8]. Currently, most approved anti-obesity drugs need to be administered once, twice, or three times daily, significantly limiting patients' treatment adherence [9]. Hence, semaglutide stands as a paramount option for future anti-obesity therapies.

Semaglutide, a glucagon-like peptide-1 receptor agonist (GLP-1 RA), operates by reducing appetite, thereby promoting better control of overeating habits and resulting in a decrease in energy intake. This mechanism of action leads to weight loss [10]. In a study involving adults being overweight or obese, the administration of subcutaneous semaglutide once a week at a dosage of 2.4 mg in conjunction with lifestyle interventions,

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Medical Research Journal 2023; 10.5603/MRJ.a2023.0034, Copyright © 2023 Via Medica, ISSN 2451-2591, e-ISSN 2451-4101

Table 1. Summary of the latest studies assessing the efficacy of subcutaneous semaglutide in adults and adolescents

Year	Author	Aim of the study	Methods	Outcome
2023	Seijas-Amigo et al. [13]	The primary endpoints included weight loss (≥ 5%), changes in weight, BMI and HbA1c upon therapy with either dulaglutide, subcutaneous semaglutide, or oral semaglutide	Out of a total of 94 participants, 42.4% were administered dulaglutide, 29.3% received subcutaneous semaglutide, and 22.8% were given oral semaglutide. Changes in weight, BMI and HbA1c were observed	Oral semaglutide was the most efficacious, with 61.1% of patients achieving weight loss. Subcutaneous semaglutide resulted in a weight loss of 45.8%, while dulaglutide yielded a weight loss of 40.6%. Overall, GLP1 RA treatment led to a significant reduction in body weight (–4.95 kg, $p < 0.001$) and BMI (–1.86 kg/m^2, $p < 0.001$)
2022	Weghuber et al. [14]	The main objectives were to assess the percentage change in BMI from the beginning of the study to week 68 and to measure the extent of weight loss, with a threshold of at least 5% achieved by week 68 upon treatment with semaglutide in obese adolescents	201 adolescents between 12 and 18 years of age with obesity or overweight with at least one weight-related coexisting condition were enrolled and subsequently divided randomly assigned to two groups: one receiving subcutaneous semaglutide, and the other being administered placebo	The average change in BMI from the start of the study to week 68 was a decrease of 16.1% for the participants receiving semaglutide, while those on placebo experienced a mere 0.6% increase (estimated difference of –16.7 percentage points; 95% CI, –20.3 to –13.2; $p < 0.001$). By week 68, a notable 73% (95 out of 131 participants) in the semaglutide group achieved a weight loss of 5% or more, compared to only 18% (11 out of 62 participants) in the placebo group (estimated odds ratio, 14.0; 95% CI, 6.3 to 31.0; $p < 0.001$)
2022	Rubino et al. [15]	The study addressed the difference between once-a--week 2.4 mg subcutaneous semaglutide *vs.* once-a-day subcutaneous 3.0 mg liraglutide in obese adults without diabetes, applying in both instances an adequate diet and physical activity	The study population consisted of 338 adults with a BMI equal to or over 30, or a BMI equal to or over 27 with at least one weight-related comorbidities. None of the patients had diabetes	The average change in weight from the starting point was a decrease of 15.8% for participants using semaglutide, whereas those using liraglutide experienced a decrease of 6.4% [a difference of –9.4 percentage points (95% CI, –12.0 to –6.8); $p < 0.001$]

BMI — body mass index; CI — confidence interval

yielded substantial weight loss, lowered the cardiometabolic risk, and improved self-reported physical functioning [9]. Notably, semaglutide at a dosage of 2.4 mg has received approval for long-term weight management when added to a reduced-calorie diet and increased physical activity for adults with obesity, as well as for overweight patients who suffer from weight-related comorbidities [11]. Recently, numerous studies have been published which revealed promising outcomes of obesity treatment with semaglutide, as shown in Table 1. Accordingly, manufacturers should strive to minimise the risk of its shortages, thus increasing the accessibility for patients who are most in need [12].

Author contributions: *Conceptualization — U.G., J.K., J.P.; methodology — U.G. and J.K.; formal analysis — U.G.; resources — U.G., J.K., J.P.; writing — original draft preparation, U.G., J.K., J.P.; writing — review and editing, U.G. and J.K.; supervision — U.G.; project administration— U.G. and J.K. All authors have read and agreed to the published version of the manuscript.*

Conflict of Interest: *None.*

Funding: *None.*

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