Tidsskriftet Tidsskrift for Den norske legeforening

The slimming jab

KARI TVEITO

kari.tveito@tidsskriftet.no
Kari Tveito, PhD, MD, specialist in internal medicine and editor of the Journal of the Norwegian Medical Association

The global community has been trying to overcome the obesity epidemic for several decades, all while people have only been getting heavier. Have we finally found the right medicine?

Photo: Einar Nilsen

Elon Musk has done it. Hollywood stars do it. A small jab in the skin once a week. That's all it takes to lose weight – at least if Twitter and Instagram are to be believed. The wonder drug has become so popular that diabetes patients who need this medication cannot get hold of it.

GLP-1 receptor agonists (glucagon-like peptide-1 receptor agonists) stimulate insulin secretion and inhibit the production of glucagon, and were initially used to treat diabetes (1). Novo Nordisk first developed liraglutide under the trade name Saxenda. Later came semaglutide, which is marketed under the name Ozempic. Semaglutide has even better efficacy than liraglutide, not least in terms of weight reduction. It quickly emerged that a useful side effect of the diabetes medication was weight loss. This is because GLP-1 receptor agonists not only slow the rate of gastric emptying, but can also suppress appetite and impact on the brain's reward system.

The latest arrival is Wegovy. Like Ozempic, Wegovy contains semaglutide, but in higher doses. In January, the Norwegian Medicines Agency rejected the use of Wegovy in the blue prescription scheme (funded by the Norwegian National Insurance Scheme) (2). The rationale was that the cost is disproportional to the benefit. Meanwhile, Saxenda, the only weight-reducing drug approved for treating obesity in adolescents, was withdrawn from the blue prescription scheme.

Worldwide, more than one billion people are overweight (BMI ≥ 25). A further 650 million are obese (BMI ≥ 30) (3). The majority of these live in low- and middle-income countries. When Novo Nordisk's Saxenda patent expires, it will be possible to produce cheaper, generic versions of liraglutide. This year, the WHO will decide whether liraglutide should be added to the list of essential medicines that are recommended for purchase in low- and middle-income countries. If it is added to the list, this will mark a new approach to the obesity epidemic.

> ***«If GLP-1 receptor agonists can prevent obesity-related cardiovascular disease and type 2 diabetes, the socioeconomic gain could nevertheless be huge»***

Can weight-reducing drugs solve the global challenges? The average weight loss when using Wegovy and making lifestyle changes is about 15 % after 68 weeks (4). This is the most dramatic effect that has ever been seen in the pharmacological treatment of obesity. Whether Wegovy prevents the development of obesity-related diseases or death is currently unknown. The ongoing SELECT study will hopefully be able to shed some light on this.

Gastrointestinal side effects are common with semaglutide (4). In rare cases, acute pancreatitis may occur. Users are also warned of a possible increased risk of thyroid cancer (5). Risks related to pregnancy have received less attention. It is recommended that women stop using semaglutide two months before pregnancy, but many pregnancies are unplanned. Women who use the

medications, and healthcare personnel who prescribe them, should be aware of the possible increased risk of adverse pregnancy outcomes, as animal studies have demonstrated reproductive toxicity (6).

What happens if you stop taking semaglutide? The weight lost is often regained (7). Not that surprising, perhaps, since obesity is a chronic, multifactorial disease. Many experts believe that it requires lifelong treatment, but that will come at a cost. If GLP-1 receptor agonists can prevent obesity-related cardiovascular disease and type 2 diabetes, the socioeconomic gain could nevertheless be huge.

The debate on blue prescriptions is also about universal, equal access to health care. African Americans and Hispanics have the highest rates of obesity in the United States. Nevertheless, very few of them are treated with weight-reducing drugs (8). Without health insurance to cover the costs, people can pay up to USD 1000 a month for the injections. Those who can afford it are rich, white Americans, who are not necessarily that overweight in the first place. Nevertheless, they still buy weight loss drugs, for example via telehealth services where a prescription can be obtained with just a few keystrokes. Fortunately, they can also afford to pay for plastic surgery if the rapid weight loss leads to a loss of subcutaneous fat and collagen in the face – the side effect that goes by the name *Ozempic face*.

In the case of morbid obesity, lifestyle changes alone are often not enough to maintain the weight loss over time (4). For this patient group, GLP-1 receptor agonists are a major therapeutic advance. Nevertheless, the cornerstone of public health work must be prevention. Taxing sugary drinks and improving access to affordable healthy foods are important measures. We need towns and cities where people can walk, run and cycle in a safe environment, and schools that promote healthy living habits from childhood. This cannot be done with a jab.

REFERENCES

1. Alruwaili H, Dehestani B, le Roux CW. Clinical Impact of Liraglutide as a Treatment of Obesity. Clin Pharmacol 2021; 13: 53–60. [PubMed][CrossRef]

2. Stranden AL. Også det etablerte fedmelegemiddelet Saxenda tas av blåresept -ordning. Forskning.no 26.1.2023. https://forskning.no/fedme-medisin/ogsa-det-etablerte-fedmelege-middelet-saxenda-tas-av-blaresept-ordning/2145750 Accessed 24.4.2023.

3. Rigby J. Exclusive: WHO to consider adding obesity drugs to essential medicines list. Reuters 29.3.2023. https://www.reuters.com/business/healthcare-pharmaceuticals/who-consider-adding-obesity-drugs-essential-medicines-list-2023-03-29/ Accessed 24.4.2023.

4. Wilding JPH, Batterham RL, Calanna S et al. Once-Weekly Semaglutide in Adults with Overweight or Obesity. N Engl J Med 2021; 384: 989–1002. [PubMed][CrossRef]

5. Bezin J, Gouverneur A, Pénichon M et al. GLP-1 Receptor Agonists and the Risk of Thyroid Cancer. Diabetes Care 2023; 46: 384–90. [PubMed] [CrossRef]

6. Relis. Semaglutideksponering i graviditet - terminere svangerskap? https://old.relis.no/sporsmal_og_svar/4-9287?source=relisdb Accessed 24.4.2023.

7. Wilding JPH, Batterham RL, Davies M et al. Weight regain and cardiometabolic effects after withdrawal of semaglutide: The STEP 1 trial extension. Diabetes Obes Metab 2022; 24: 1553–64. [PubMed][CrossRef]

8. Edwards E. As weight loss drugs soar in popularity, many who could benefit can't get them. NBC News 3.2.2023. https://www.nbcnews.com/health/health-news/ozempic-wegovy-weight-loss-drugs-demand-soars-rcna68425 Accessed 24.4.2023.

Publisert: 8 May 2023. Tidsskr Nor Legeforen. DOI: 10.4045/tidsskr.23.0304