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Commentary

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Possible Adverse Effects (AEs) of Semaglutide (Ozempic) Administration for the Latest Investigation

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Abstract

Semaglutide has been widely used in the treatment of type 2 diabetes (T2D) and obesity within medical and healthcare settings. Among its formulations, Ozempic has drawn attention for potential adverse effects (AEs). In a study involving 3,962 cases of obesity, the average data showed a weight reduction of 11.8%, a BMI decrease of 4.5 kg/m^2, and a reduction in waist circumference of 9.4 cm. One notable effect, termed "Ozempic tongue," is characterized by altered taste sensitivity—such as sour, metallic, or bitter tastes—reported in approximately 6% of cases. These effects are not only considered AEs but are also linked to beneficial outcomes in weight reduction. Additionally, some users have reported changes in the appearance of the breasts, buttocks, and lips with Ozempic administration.

Keywords

Semaglutide, Adverse Effects (AE), Ozempic Tongue, Tirzepatide, FDA Adverse Event Reporting System (FAERS)

Commentary

Recently, Glucagon-Like Peptide-1 receptor agonists (GLP-1RAs) have been widely used for the treatment of type 2 diabetes (T2D) and obesity in medical and healthcare regions. Among them, clinical effects and adverse effects (AE) have attracted attention. The latest impressive topics will be described in this article. It has been known that semaglutide lowers blood glucose levels and leads to significant weight reduction. A systematic review was conducted, and the primary outcomes were all-cause mortality and adverse events [1]. Secondary outcomes were myocardial infarction, stroke, all-cause hospitalization, and non-serious adverse events. Lots of data came from compared data, including the Semaglutide Effects on Cardiovascular Outcomes in People with Overweight or Obesity (SELECT) trial [2].

Concerning the AE of semaglutide for different routes, the event profiles were compared using the reporting of the FDA in the US [3]. Data was collected from the US FDA Adverse Event Reporting System (FAERS) database for 2017-2023. As a result, a total of 22,287 records were identified from FAERS. Comparative analyses were conducted for the subcutaneous route (n=16,346) and the oral route (n=2,496). Different administrations may bring varying outcomes. The former seemed to have AE with the endocrine system, and the latter seemed to bring gastrointestinal AE. Then, semaglutide presented

variations of AE based on the administration route.

For decades, obesity has been a global health problem, and it has few pharmacologically effective options. Its essential treatment would be weight reduction, which leads to improved outcomes for obesity and T2D [4]. From SURMOUNT-2 research for GLP-1RA, adverse events were observed for the GI tract without psychiatric adverse events [5]. In experiments on animal models, semaglutide showed antidepressant and anxiolytic efficacy. The safety committee of the European Medicine Agency (EMA) and the Pharmacovigilance Risk Assessment Committee (PRAC) have shown reviewed data for the possible risk for suicide or self-harm using GLP-1RA [6]. Thus, GLP-1RA should be applied with attention and monitored for the risk of psychological and psychiatric problems.

Semaglutide has been widely used for type 2 diabetes (T2D) and obesity in medical and healthcare regions. Among them, Ozempic has been reported for its possible adverse effects (AE), attracting attention. For 3,962 obesity cases, average data showed a weight reduction of -11.8%, a BMI decrease of -4.5 kg/m^2, and a waist circumference reduction of -9.4 cm.

The latest systematic review and meta-analysis of semaglutide was conducted for 6 RCTs with 3,962 obesity cases [7]. As a result, -11.8% for the reduction ratio of body weight, -12.2 kg for absolute weight decrease, -4.5 kg/m^2 for BMI, and -9.4 cm for waist circumference were found. In contrast, the most common AE was gastrointestinal adverse effects (GI-AE) with a risk ratio of 1.49. Among some brand names of semaglutide, Ozempic has been known for its significant weight reduction efficacy, but also for some AE. Some reports have observed side effects as Ozempic breasts, butt, lips, and tongue [8]. As oral AE of Ozempic, dry mouth, halitosis, and dysgeusia were found; certain researchers have reported a novel development of sweet taste in the mouth, called Ozempic tongue. In patients with obesity, cravings for sugary-tasting food may be linked to elevated leptin levels, which can reduce the perceived degree of sweet tastes. Furthermore, semaglutide administration like Ozempic would reverse such clinical effects by elevated sensitivity to sweet flavors.

From the systematic review, obesity may influence taste perception and also the brain reward response system for specific tastes, which can elevate cravings for fatty and sweet foods and decrease taste sensitivity because of increased leptin levels [9]. Recently, GLP-1RA is known to decrease cravings for sweet, sugary foods or alcoholic beverages. According to recent research, Ozempic may give cases different taste sensitivity, called Ozempic tongue. This means that the case will feel sour, metallic, or bitter tastes that are different from before. Such a phenomenon may discourage the case from eating these types of foods, which can lead to smooth weight reduction.

Regarding Ozempic tongue, it does not necessarily mean AE or an inadequate phenomenon. Such a changed taste sensation or dysgeusia may develop as early as about two weeks after initiating semaglutide, and it can be found in up to 6% of cases with Ozempic therapy [10]. Thus, a change in taste sensation would be considered one of the AE, as well as decreased appetite. However, these effects seem to have a rather beneficial tendency for achieving weight reduction and improved glucose variability. Until now, the detailed mechanism for this taste change remains unclear. Ozempic may alter the gene related to taste receptors on the tongue, but there is no apparent reason or theory that can explain these clinical symptoms. The related mechanism will hopefully be clarified in the near future.

Semaglutide would influence not only the gastrointestinal (GI) axis, but also the renal-cardiometabolic axes. It would affect GLP-1 receptors in the brain, which are involved in diuretic, water intake, and natriuretic mechanisms, and decrease renal angiotensin II values. Such a mechanism may bring chronic diarrhea, diuresis, nasopharyngitis, and xerostomia. Furthermore, semaglutide can lead to frothy saliva and mouth dryness [11]. This will bring halitosis, which is called Ozempic breath. In addition, eructation may develop as another common AE, leading to halitosis [12]. Obesity causes certain sarcopenia in the genioglossal muscle associated with an increased amount of tongue fat, which may benefit obesity-associated sleep apnea. Related to these phenomena, a pilot study found that semaglutide could significantly decrease the fat amount on the tongue [13].

Historically, Ozempic was approved by the FDA in the US for treating T2D in 2017. Weight reduction was a noted AE, but after that, many people wanted it for the purpose of weight reduction. Then, online scammers have targeted some people who seek to obtain such drugs through fake websites, advertising, or social media posts [14]. The latest data shows about a 183% increase in these scams during the first quarter of 2024.

Regarding the latest attraction, a comparison of the clinical effects between semaglutide and tirzepatide has been reported [15]. In 18,386 cases from 41,222 applicants, the tirzepatide group showed a higher ratio of weight reduction than semaglutide. The hazard ratio (HR) showed 1.76 (in ≥5% reduction cases), 2.54 (in ≥10%), and 3.24 (in ≥15%). Psychiatric AE were investigated for GLP-1RA, including semaglutide, tirzepatide, and liraglutide [16]. The research included 31,444 cases, in which AE were reported for 372 (1.18%). Among them, there was depression (n=187, 50.3%), anxiety (n=144), and suicidal ideation (n=73). Consequently, the current study showed a 1.2% adverse event rate for the three kinds of GLP-1RA. Future detailed investigations would be required for the severity of adverse events.

In summary, the latest topics concerning GLP-1RA, semaglutide, Ozempic, and tirzepatide have been introduced in this article. We can expect further research and development to clarify the detailed mechanisms related to medical practice.

Conflict of Interest

The author has read and approved the final version of the manuscript. The author has no conflicts of interest to declare.

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References

[1] Sillassen CDB, Kamp CB, Petersen JJ, Faltermeier P, Siddiqui F, Grand J, Dominguez H, Frølich A, Gæde PH, Gluud C, Mathiesen O, Jakobsen J. Adverse effects with semaglutide: a protocol for a systematic review with meta-analysis and trial sequential analysis. BMJ Open. 2024 Jun 21;14(6):e084190. [**PMID**: 3890883]

[2] Lincoff AM, Brown-Frandsen K, Colhoun HM, Deanfield J, Emerson SS, Esbjerg S, Hardt-Lindberg S, Hovingh GK, Kahn SE, Kushner RF, Lingvay I, Oral TK, Michelsen MM, Plutzky J, Tornøe CW, Ryan DH; SELECT Trial Investigators. Semaglutide and Cardiovascular Outcomes in Obesity without Diabetes. N Engl J Med. 2023 Dec 14;389(24):2221-32. [**PMID**: 37952131]

[3] Niu K, Fan M, Gao W, Chen C, Dai G. Adverse events in different administration routes of semaglutide: a pharmacovigilance study based on the FDA adverse event reporting system. Front Pharmacol. 2024 Jun 3;15:1414268. [**PMID**: 38887555]

[4] Wang JY, Wang QW, Yang XY, Yang W, Li DR, Jin JY, Zhang HC, Zhang XF. GLP-1 receptor agonists for the treatment of obesity: Role as a promising approach. Front Endocrinol (Lausanne). 2023 Feb 1;14:1085799. [**PMID**: 36843578]

[5] Garvey WT, Frias JP, Jastreboff AM, le Roux CW, Sattar N, Aizenberg D, Mao H, Zhang S, Ahmad NN, Bunck MC, Benabbad I, Zhang XM; SURMOUNT-2 investigators. Tirzepatide once weekly for the treatment of obesity in people with type 2 diabetes (SURMOUNT-2): a double-blind, randomised, multicentre, placebo-controlled, phase 3 trial. Lancet. 2023 Aug 19;402(10402):613-26. [**PMID**: 37385275]

[6] European Medicine Agency (EMA). EMA statement on ongoing review of GLP-1 receptor agonists. European Medicine Agency – Science Medicines Health. 2023 Jul 11 [cited 2023 Aug 15]. Available from: https://www.ema.europa.eu/en/news/ema-statement-ongoing-review-glp-1-receptor-agonists

[7] Qin W, Yang J, Deng C, Ruan Q, Duan K. Efficacy and safety of semaglutide 2.4 mg for weight loss in overweight or obese adults without diabetes: An updated systematic review and meta-analysis including the 2-year STEP 5 trial. Diabetes Obes Metab. 2024 Mar;26(3):911-23. [**PMID**: 38016699]

[8] Mohta H, Goetz H. Ozempic tongue' and other oral side effects explained. MDLinx. 2024 July 24.

[9] Fathi M, Javid AZ, Mansoori A. Effects of weight change on taste function; a systematic review. Nutr J. 2023 May 8;22(1):22. [**PMID**: 37158889]

[10] Volpe S, Lisco G, Fanelli M, Racaniello D, Colaianni V, Lavarra V, Triggiani D, Crudele L, Triggiani V, Sabbà C, De Pergola G, Piazzolla G. Oral semaglutide improves body composition and preserves lean mass in patients with type 2 diabetes: a 26-week prospective real-life

study. Front Endocrinol (Lausanne). 2023 Sep 13;14:1240263. [**PMID**: 37780624]

[11] Mawardi HH, Almazrooa SA, Dakhil SA, Aboalola AA, Al-Ghalib TA, Eshky RT, Niyazi AA, Mawardi MH. Semaglutide-associated hyposalivation: A report of case series. Medicine (Baltimore). 2023 Dec 29;102(52):e36730. [**PMID**: 38206684]

[12] Shu Y, He X, Wu P, Liu Y, Ding Y, Zhang Q. Gastrointestinal adverse events associated with semaglutide: A pharmacovigilance study based on FDA adverse event reporting system. Front Public Health. 2022 Oct 20;10:996179. [**PMID**: 36339230]

[13] Jensterle M, Ferjan S, Vovk A, Battelino T, Rizzo M, Janež A. Semaglutide reduces fat accumulation in the tongue: A randomized single-blind, pilot study. Diabetes Res Clin Pract. 2021 Aug;178:108935. [**PMID**: 34217774]

[14] Srakocic S, Sherman D. Scams involving Ozempic, Mounjaro, and Wegovy increase. Specialties & Diseases. MD Linx. 2024 June 25.

[15] Rodriguez PJ, Goodwin Cartwright BM, Gratzl S, Brar R, Baker C, Gluckman TJ, Stucky NL. Semaglutide vs Tirzepatide for Weight Loss in Adults with Overweight or Obesity. JAMA Intern Med. 2024 Sep 1;184(9):1056-1064. [**PMID**: 38976257]

[16] Tobaiqy M, Elkout H. Psychiatric adverse events associated with semaglutide, liraglutide and tirzepatide: a pharmacovigilance analysis of individual case safety reports submitted to the EudraVigilance database. Int J Clin Pharm. 2024 Apr;46(2):488-95. [**PMID**: 38265519]

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