GLP-1 Receptor Agonists: Understanding Oral Manifestations

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The widespread adoption of glucagon-like peptide-1 (GLP-1) receptor agonists for type 2 diabetes and weight management has brought increased attention to their systemic effects. While their efficacy in glycaemic control and weight reduction is well-established, clinicians should be aware of emerging reports concerning oral health manifestations, colloquially termed 'Ozempic Mouth', which primarily involve xerostomia and its sequelae.

KEY TAKEAWAYS

- The Pivot: GLP-1 receptor agonists, while effective for metabolic conditions, are increasingly linked to specific oral health challenges.
- The Data: Xerostomia, a common adverse effect, can lead to increased dental caries risk and periodontal disease.
- The Action: Clinicians should proactively counsel patients on potential oral adverse effects and recommend preventive dental care strategies.

GLP-1 receptor agonists, including semaglutide and liraglutide, function by mimicking the endogenous incretin hormone GLP-1, thereby enhancing glucose-dependent insulin secretion, suppressing glucagon secretion, slowing gastric emptying, and promoting satiety.1 These mechanisms contribute to their therapeutic benefits in managing type 2 diabetes and obesity. However, the slowing of gastric emptying, a key mechanism of action, is also associated with common gastrointestinal adverse effects such as nausea, vomiting, and constipation.2 The clinical utility of GLP-1 receptor agonists has expanded significantly, moving from a niche treatment for type 2 diabetes to a widely adopted therapy for weight management in individuals with obesity or overweight with comorbidities. This expansion has led to a larger and more diverse patient population receiving these medications, increasing the importance of understanding their full spectrum of adverse effects, including those affecting oral health.

Beyond gastrointestinal effects, a less frequently discussed but clinically relevant adverse effect is xerostomia, or dry mouth.3 While not universally reported in initial pivotal trials as a primary endpoint, post-marketing surveillance and anecdotal reports have highlighted its prevalence. Xerostomia can arise from various causes, including medication side effects, systemic diseases, and salivary gland dysfunction.4 In the context of GLP-1 receptor agonists, the exact pathophysiology of drug-induced xerostomia is not fully elucidated, but it is hypothesised to be related to altered autonomic nervous system activity or direct effects on salivary gland function.5 The prevalence of xerostomia in the general population varies but is estimated to affect approximately 10-30% of adults, with higher rates in older individuals and those taking multiple medications. For patients on GLP-1 receptor agonists, the incidence of xerostomia appears to be higher than in placebo groups in some studies, though specific rates can vary depending on the drug, dosage, and

duration of treatment. Understanding this background prevalence is crucial for clinicians to differentiate drug-induced xerostomia from other causes and to manage patient expectations effectively.

Oral Manifestations and Management Strategies

Chronic xerostomia can have significant implications for oral health. Saliva plays a critical role in maintaining oral homeostasis by lubricating oral tissues, aiding in food bolus formation, facilitating taste, and providing antimicrobial protection.6 A reduction in salivary flow and changes in salivary composition can lead to several adverse outcomes. Patients experiencing xerostomia are at an increased risk of dental caries due to reduced buffering capacity and impaired clearance of food debris and acids from the tooth surface.7 Furthermore, the lack of salivary lubrication can result in discomfort, difficulty speaking and swallowing (dysphagia), and an increased susceptibility to oral mucosal infections, such as candidiasis.8 Periodontal disease progression may also be exacerbated in individuals with chronic dry mouth.9 These oral manifestations can significantly impair a patient's quality of life, affecting nutrition, social interactions, and overall well-being. The long-term consequences of untreated xerostomia can include extensive dental restorative needs and increased susceptibility to systemic infections originating from the oral cavity.

Management of GLP-1 receptor agonist-associated xerostomia involves a multi-faceted approach focused on symptom relief and prevention of sequelae. Patients should be advised to maintain meticulous oral hygiene, including regular brushing with fluoride toothpaste and daily flossing.10 Frequent sips of water throughout the day can help alleviate dryness. Over-the-counter salivary substitutes, such as artificial saliva sprays or gels, can provide temporary relief.11 Sugar-free chewing gum or lozenges can stimulate salivary flow, provided they do not contain ingredients that could exacerbate dental erosion.12 For patients with severe or persistent symptoms, prescription medications such as pilocarpine or cevimeline, which stimulate salivary gland secretion, may be considered, though their use should be weighed against potential systemic adverse effects.13 Regular dental check-ups, ideally every three to six months, are crucial for early detection and management of dental caries or periodontal issues.14 Dental professionals may recommend topical fluoride applications or high-fluoride toothpastes to enhance remineralisation and reduce caries risk.15 The management strategy should be tailored to the individual patient's symptoms, oral health status, and overall medical profile. Patient education regarding the potential for xerostomia and its oral health implications is paramount for proactive management and prevention of severe complications. Limitations in current research include a lack of large-scale, prospective studies specifically designed to evaluate the incidence and severity of xerostomia as a primary endpoint in GLP-1 receptor agonist trials, which would provide more definitive epidemiological data and insights into specific patient populations at higher risk.

> **CLINICAL IMPLICATIONS**
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> The emergence of 'Ozempic Mouth' as a recognised adverse effect of GLP-1 receptor agonists underscores the importance of a holistic approach to patient care. While the metabolic benefits of these agents are substantial, clinicians must integrate potential oral health consequences into their prescribing discussions. It is insufficient to merely focus on HbA1c or weight reduction; patient quality of life, including oral comfort and dental health, warrants equal consideration.
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> For primary care physicians and endocrinologists, this means proactively inquiring about oral dryness and associated symptoms during follow-up appointments. A simple question can prompt a discussion that leads

> to early intervention, potentially preventing significant dental morbidity. Collaboration with dental professionals is also paramount. Establishing clear referral pathways and encouraging patients to inform their dentists about their medication regimen can facilitate tailored preventive strategies. The pharmaceutical industry, in turn, should ensure that comprehensive information regarding oral adverse effects, including management strategies, is prominently featured in prescribing information and patient education materials. This is not merely a matter of regulatory compliance but of ethical responsibility to the millions of patients now using these therapies.
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> Ultimately, the long-term success of GLP-1 receptor agonists hinges not only on their efficacy but also on the effective management of their adverse effect profile. Neglecting oral health concerns could diminish patient adherence and overall satisfaction, despite the profound metabolic improvements. A proactive, interdisciplinary approach is essential to ensure that the benefits of these innovative treatments are fully realised without compromising other aspects of patient well-being.

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