Review Article

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Oral Health Manifestations of GLP-1 and Dual GIP/GLP-1 Receptor Agonist Therapies (Semaglutide and Tirzepatide): A Review

Abstract:
The global surge in glucagon-like peptide-1 (GLP-1) receptor agonists and dual incretin therapies, such as semaglutide (Ozempic) and tirzepatide (Mounjaro), has introduced distinct secondary oral complications widely recognized as "Ozempic Mouth" and "Ozempic Teeth." Immediate therapy triggers severe salivary hypofunction and accelerated gastric reflux across both drug classes, while long-term maintenance promotes profound structural damage, including severe enamel decay, dental restoration failure, and the facial soft tissue hollowing known as "Ozempic Face." Dental practitioners must recognize these shared clinical manifestations and employ targeted remineralization, acid neutralization, and pre-surgical protocols to protect dental health during metabolic treatment.

Key-words: Semaglutide; Tirzepatide; Ozempic; Mounjaro; GLP-1 receptor agonists; Xerostomia; Dental Erosion; Periodontal Health.

Introduction:

The medical landscape for metabolic disorders and chronic obesity has shifted dramatically with the introduction of glucagon-like peptide-1 receptor agonists (GLP-1 RAs) and dual incretin therapies, primarily represented by **semaglutide (Ozempic)** and **tirzepatide (Mounjaro)** [1]. While semaglutide operates as a selective single GLP-1 receptor agonist, tirzepatide represents a novel class of synthetic polypeptides that functions as a dual agonist for both the GLP-1 and glucose-dependent insulinotropic polypeptide (GIP) receptors [1,2]. Both drug classes demonstrate exceptional glycemic control and profound, dose-dependent weight reduction in clinical settings [1]. However, as clinical adoption scales globally, the dental community is increasingly observing secondary oral health complications across patients taking either medication [2]. These complications can be categorised into acute, immediate physiological changes and progressive, long-term structural risks [2,3].

In the immediate phase of therapy for both semaglutide and tirzepatide, patients often report rapid-onset **xerostomia (dry mouth)** and altered gustatory perception (dysgeusia) [3,4]. Saliva is the oral cavity's primary innate defence system, responsible for buffering bacterial acids, maintaining a balanced oral microbiome, and facilitating tissue repair [4]. Transcriptomic and molecular data have confirmed that GLP-1 receptors are functionally expressed within mammalian salivary glands [5]. The continuous receptor activation induced by both weekly semaglutide and tirzepatide appears to cause prolonged stimulation of these pathways [5]. This

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disrupts the homeostatic intracellular calcium and cAMP cross-talk required for normal salivary secretion, causing severe subjective and objective hyposalivation within weeks of initiating therapy [3,5]. Compounding this, the immediate gastrointestinal side effects shared by these medications—namely nausea, vomiting, and severely delayed gastric emptying—frequently exacerbate **gastroesophageal reflux disease (GERD)** [1,6]. This shifts the oral environment to a highly acidic state (pH < 5.5), putting patients at an immediate risk for dentinal hypersensitivity and mucosal inflammation across both treatment regimens [6,7].

Over the long term, these continuous acute challenges manifest as permanent structural damage regardless of the specific incretin agent utilized. Prolonged hyposalivation dramatically compromises **dental restoration longevity**, accelerating secondary caries around margins and causing composite or glass ionomer fillings to fail prematurely [3,8]. Chronic, unmitigated exposure to gastric acids leads to irreversible **enamel erosion**, thinning incisal edges, and extensive tooth demineralization [6,9]. Furthermore, the extreme appetite suppression induced by both single and dual incretin agonism can lead to persistent nutritional deficiencies in calcium, vitamin D, and vitamin C [2,10]. These elements are critical for maintaining periodontal attachment apparatus integrity and alveolar bone density [10]. This narrative review aims to synthesise the immediate physiological shifts and long-term pathodontic outcomes associated with semaglutide and tirzepatide therapies, offering a clear, evidence-based management protocol for dental practitioners navigating this rapidly expanding patient demographic.

Immediate Oral Health Effects of Incretin Mimetic Therapy:

The immediate or acute phase of semaglutide and tirzepatide therapies—typically spanning the first 4 to 12 weeks of treatment or occurring during periods of active dose escalation—is characterized by rapid physiological disruptions within the oral cavity. These changes occur as a direct consequence of GLP-1 and GIP receptor agonism, which alters autonomic regulation and upper gastrointestinal kinetics.

Acute Salivary Gland Hypofunction and Xerostomia:

The most immediate and universally reported oral complaint following the initiation of these medications is severe xerostomia accompanied by objective hyposalivation [3,11]. Saliva production is regulated via autonomic parasympathetic (muscarinic) and sympathetic (adrenergic) signaling pathway cross-talk [5]. Because GLP-1 receptors are functionally active within the epithelial cells of the salivary ducts and acini, the continuous presence of long-acting agonists like semaglutide or tirzepatide disrupts this delicate homeostatic balance.

Within days of therapeutic initiation, patients experience a profound drop in resting and stimulated salivary flow rates. This acute deficiency strips the oral mucosa of its protective salivary pellicle, leading to immediate clinical complications:

- **Mucosal Friability:** The oral soft tissues become erythematous, dry, and highly susceptible to mechanical trauma during mastication.
- **Early Microbial Shifts:** The loss of antimicrobial proteins (such as secretory IgA, lysozyme, and lactoferrin) allows for the rapid colonization of opportunistic pathogens, leading to an immediate spike in acute oral candidiasis (thrush) and angular cheilitis at the commissures of the lips.
- **Dysgeusia and Glossodynia:** Patients frequently describe a burning tongue sensation (glossodynia) or a persistent metallic, bitter taste (dysgeusia). This is triggered by a combination of reduced chemical dissolution of tastants in saliva and direct neurochemical changes in taste bud receptor cells.

Chemical Enamel Demineralization and GERD:

Simultaneously, the immediate upper gastrointestinal side effects of semaglutide and tirzepatide present a severe chemical challenge to dental structures. These agents achieve their metabolic efficacy partly by significantly delaying gastric emptying to prolong postprandial satiety. Clinically, this gastric stagnation causes a substantial increase in intra-abdominal pressure, resulting in acute, severe GERD, chronic nausea, and episodic vomiting.

During these episodes, the oral cavity is repeatedly flooded with gastric contents possessing a highly destructive pH ranging from 1.5 to 2.0. This shifts the local oral environment far below the critical pH threshold of hydroxyapatite (pH 5.5) and fluorapatite (pH 4.5). Because this acid challenge coincides with the aforementioned lack of buffering saliva, immediate enamel demineralization occurs. Patients typically present within weeks complaining of sudden-onset, severe dentinal hypersensitivity, particularly on the palatal and

lingual surfaces of the maxillary anterior teeth where gastric acid directly pools.

Long-Term Manifestations on the Salivary Microenvironment and Gastrointestinal Dynamics:

As semaglutide and tirzepatide therapies transition from acute titration to long-term maintenance, the prolonged suppression of salivary function permanently alters oral homeostasis [11]. Over extended periods, chronic hyposalivation forces a pathological shift in the salivary microenvironment [12]. The sustained lack of serous salivary flow reduces the concentration of critical inorganic ions, such as calcium and phosphate, which are indispensable for continuous, microscopic enamel remineralization [4].

Concurrently, the biochemical profile of the remaining saliva changes; a lower flow rate reduces the secretion of bicarbonate ions, significantly undermining the mouth's natural buffering capacity [12]. This chronic fluid deficit creates a highly localized, acidic, and anaerobic environment. Under these conditions, the oral microbiome experiences a dysbiotic shift, favoring the proliferation of aciduric and cariogenic strains such as *Streptococcus mutans* and *Lactobacillus* species over protective commensal microflora [10].

This microenvironmental breakdown is continually exacerbated by long-term gastrointestinal dynamics. The delayed gastric emptying induced by incretin receptor agonism is not a transient side effect; it often persists throughout the maintenance phase of the medication [13]. Consequently, patients suffer from chronic, low-grade nocturnal regurgitation and silent gastroesophageal reflux [6,14]. This continuous, micro-exposure to gastric acids means that even during sleep—when natural salivary flow is already at its physiological lowest—the dentition is subjected to unmitigated chemical attack, solidifying the pathodontic framework for extensive structural decay [6,11].

Hard Tissue Erosion and Structural Breakdown:

The compounding impact of chronic acid exposure and a compromised salivary microenvironment manifests as severe hard tissue erosion and progressive structural failure of the dentition [9]. Pathological enamel erosion, or perimylolysis, becomes highly visible during long-term clinical examinations [6]. As the outer aprismatic enamel is slowly stripped away by recurring chemical insults, the softer, underlying dentin is exposed [4]. Dentin demineralizes at a much higher critical pH threshold (pH 6.2 to 6.7) than enamel, leading to an accelerated rate of hard tissue destruction once the protective outer layer is breached [4,6].

Clinically, this structural breakdown presents with distinct morphological landmarks:

- **Cupping and Guttering:** The occlusal surfaces of molars exhibit smooth, rounded depressions (cupping), and the incisal edges of anterior teeth thin out, presenting a translucent, brittle, or jagged appearance [6,9].
- **Restoration Marginal Failure:** Dental restorations lose their structural integrity. Because composite resins, glass ionomer cements, and dental amalgams rely on sound, surrounding tooth structure for marginal sealing, the systemic erosion of adjacent enamel creates severe microleakage [8]. This leads to a high incidence of recurrent, secondary dental caries around existing margins, culminating in premature restoration failure and the need for complex, multi-surface prosthetic interventions [3,8].

Systemic Metabolic Shifts vs. Periodontal Health:

While the superficial structures of the teeth face severe chemical and microbial degradation, the deeper supporting tissues are governed by the systemic metabolic shifts induced by semaglutide and tirzepatide. Long-term use of these incretin agonists yields profound systemic transformations, including rapid adipose tissue depletion, altered lipid profiles, and improved insulin sensitivity [1,13]. However, the extreme appetite suppression can inadvertently introduce secondary challenges to the periodontium through nutritional restriction [2].

During rapid weight loss phases, patients frequently fall into states of subclinical malnutrition, exhibiting deficient intake of essential micronutrients like Vitamin C (ascorbic acid) and Vitamin D3 (cholecalciferol) [15]. Vitamin C is an absolute requirement for collagen synthesis and the maintenance of the periodontal ligament; its deficiency impairs the structural integrity of the capillary beds within the gingival tissues, leading to increased gingival friability and bleeding upon probing, independent of local plaque accumulation [15].

Simultaneously, long-term Vitamin D3 and calcium deficiencies disrupt systemic bone remodeling kinetics [16]. In the oral cavity, this can manifest as a subtle reduction in

alveolar bone density [10,16]. A compromised alveolar bone bed, when paired with the hyper-inflammatory potential of an acid-induced dysbiotic oral microbiome, accelerates the progression of chronic periodontitis [10]. This can result in increased clinical attachment loss, pathological tooth mobility, and a higher failure rate for osseointegrated dental implants due to a weakened skeletal foundation [8,16].

Clinical Management Protocols for Dental Practitioners:

To effectively counteract the pathogenic pathway initiated by incretin receptor agonism, dental professionals must transition from reactive treatment to an aggressive, preventive medical model.[17] Management is structured around chemical enamel protection, salivary enhancement, and multi-disciplinary medical coordination.[17]

1. Chemical and Mechanical Enamel Stabilization

- **High-Potency Fluoride Therapy:** Patients should be immediately transitioned to an at-home 5000-ppm neutral sodium fluoride toothpaste to stimulate remineralization of compromised smooth surfaces [1,3,17]. Additionally, professional topical application of 5% sodium fluoride varnish should be rendered every 3 to 4 months during recall visits [1,3].
- **The 60-Minute Post-Emesis Protocol:** To prevent the mechanical abrasion of acid-softened hydroxyapatite, patients must be strictly counseled against brushing their teeth immediately after a reflux or vomiting episode [6,14]. Instead, they should rinse immediately with a neutralizing sodium bicarbonate solution (one teaspoon of baking soda dissolved in eight ounces of water) to drive the oral pH back above the critical threshold [6,14]. Brushing should be delayed for a minimum of 60 minutes.[17]
- **Amorphous Calcium Phosphate (ACP):** Casein phosphopeptide-amorphous calcium phosphate (CPP-ACP) topical pastes should be applied nightly to provide a supersaturated reservoir of calcium and phosphate ions within the remaining salivary pellicle.

2. Xerostomia and Salivary Microenvironment Interventions:

- **Sialagogues and Xylitol Delivery:** The use of therapeutic, sugar-free chewing gums or lozenges containing high doses of **xylitol** is highly recommended [2,4]. Xylitol serves a dual function: it stimulates residual parasympathetic salivation while actively downregulating the proliferation of cariogenic *Streptococcus mutans* [2,4].
- **Saliva Substitutes:** For patients experiencing profound nocturnal hyposalivation, carboxymethylcellulose or mucin-based oral sprays and lubricating gels should be applied directly to the oral mucosa prior to sleep to protect against silent, nighttime GERD [12,14].
- **Antifungal Prophylaxis:** Given the high incidence of opportunistic infections secondary to decreased salivary IgA, practitioners should monitor closely for candidiasis and prescribe topically active nystatin suspensions or clotrimazole troches at the earliest clinical sign of mucosal erythema or angular cheilitis.

3. Interdisciplinary Care and Perioperative Protocols:

- **Nutritional Surveillance:** Dentists should maintain an open line of communication with the patient's prescribing physician or registered dietitian [2]. Routine screening should verify adequate systemic levels of Vitamin C, Vitamin D3, and calcium to prevent accelerated alveolar bone loss or periodontal structural breakdown [15,16].
- **Pre-Surgical Gastric Emptying Precautions:** For any patient scheduled for elective dental surgery requiring deep sedation or general anesthesia, the dental team must enforce specialized screening [5,8]. Due to drug-induced delayed gastric emptying, current guidelines recommend holding weekly formulations (both semaglutide and tirzepatide) for **one full week** prior to anesthesia to minimize the life-threatening risk of pulmonary aspiration [5]. If surgery cannot be delayed, full-stomach anesthetic precautions must be systematically employed [8].

Conclusion:

Semaglutide (Ozempic) and tirzepatide (Mounjaro) represent major breakthroughs in metabolic medicine, yet their secondary impact on oral health requires immediate, structured intervention from the dental community. These medications compromise the oral cavity through a shared dual pathway: an immediate destruction of the salivary

microenvironment coupled with aggressive, chronic acid exposure from delayed upper gastrointestinal kinetics. Over time, this pipeline drives the dentition toward severe hard tissue erosion, widespread restoration failure, and potential periodontal attachment loss.

Ultimately, these manifestations are not a result of direct pharmacological toxicity to dental hard tissues, but rather the predictable systemic consequences of prolonged incretin agonism. By adopting the comprehensive management protocols outlined in this review—prioritizing acid neutralization, high-potency topical remineralization, and strict perioperative safety measures—dental practitioners can effectively preserve oral health, ensuring that their patients achieve metabolic success without sacrificing their dental integrity.

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