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Periodontal Health Decline in Diabetic Patients: Clinical Reports, Cytokine Analysis, and Antidiabetic Therapies

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Abstract: ***Diabetes mellitus induces chronic hyperglycemia and systemic inflammation, leading to periodontal deterioration characterized by gingival inflammation, bone loss, and deep periodontal pockets. This review explores the pathophysiological mechanisms linking diabetes and periodontal disease, focusing on inflammatory cytokines (TNF-α, IL-1β, and IL-6) and their role in disease progression. Five clinical case reports illustrate how different antidiabetic medications metformin, insulin, DPP-4 inhibitors, GLP-1 receptor agonists, and SGLT2 inhibitors affect periodontal healing. Special attention is given to Rybelsus, a novel oral GLP-1 receptor agonist, in comparison with other treatments. Findings highlight the necessity of multidisciplinary treatment strategies and strict glycemic control for improving periodontal health in diabetic patients.***

Keywords: Diabetes, Periodontal Health, Inflammation, Cytokines, Rybelsus, Antidiabetic Therapy

1. Introduction

Diabetes mellitus is a critical public health issue with rising prevalence and associated complications. Chronic hyperglycemia triggers oxidative stress, systemic inflammation, immune dysfunction, and increased protein glycosylation, all of which contribute to alterations in the structure of gingival tissues (American Diabetes Association, 2020; Varki, 1993). The bidirectional relationship between diabetes and periodontal disease means that poor glycemic control worsens periodontal deterioration, while severe periodontal infections further complicate diabetes management.

This study aims to evaluate periodontal deterioration in diabetic patients by analyzing inflammatory cytokine activity, reviewing clinical case reports, and comparing the effects of antidiabetic medications, with a special focus on Rybelsus.

2. Pathophysiological Mechanisms

2.1 Inflammatory Response and Pro-inflammatory Cytokines

Chronic hyperglycemia in diabetic patients leads to increased production of pro-inflammatory cytokines in the gingival tissue, including TNF-α, IL-1β, and IL-6.

- TNF-α: Elevated levels of TNF-α accelerate collagen degradation, leading to gingival recession, bone erosion, and the deepening of periodontal pockets (Taylor & Borgnakke, 2008).
- IL-1β and IL-6: These cytokines further amplify local inflammation, contributing to progressive tissue destruction.

2.2 Glycosylation and Advanced Glycation End-Products (AGEs)

The hyperglycemic environment enhances non-enzymatic glycosylation of proteins, resulting in the formation of AGEs. AGEs contribute to microvascular damage, increased rigidity of the connective tissue, and perpetuation of chronic inflammation within periodontal tissues.

2.3 Immune Dysregulation

Diabetes adversely affects neutrophil and macrophage functions and disrupts antibody production, thereby weakening the host's defense against periodontal pathogens. This immune compromise allows pathogenic bacteria to proliferate, further intensifying local inflammatory responses.

3. Clinical Case Reports and Antidiabetic Medication Use

In this section, we present five clinical case reports in which the patients' antidiabetic treatment regimens are integrated with periodontal management strategies. Additionally, it examines how various antidiabetic medications influence periodontal healing, with a particular focus on Rybelsus, an oral GLP-1 receptor agonist, and its effectiveness in reducing inflammation and improving periodontal outcomes.

Case 1: Middle-Aged Patient with Moderate Periodontal Destruction

A 52-year-old male patient with an 8-year history of type 2 diabetes presented with moderate periodontal destruction. His fasting blood glucose was measured at 190 mg/dL, and his HbA1c level was 8.5%. A periodontal examination revealed the presence of 4–5 mm periodontal pockets, mild gingival recession, and localized inflammation, while radiographic imaging demonstrated a slight reduction in bone density. The patient was undergoing treatment with metformin for systemic glycemic control, which also contributed to reducing pro-inflammatory cytokines such as TNF-α and IL-6, thereby supporting periodontal healing. As part of the treatment strategy, local debridement, including scaling and root planning, was performed alongside reinforcement of oral hygiene practices. Additionally, low-dose nonsteroidal anti-inflammatory drugs (NSAIDs) were administered for inflammation control. At the three-month follow-up, a significant improvement in periodontal parameters was observed, accompanied by better glycemic control.

Case 2: Elderly Patient with Long-Standing Diabetes and Advanced Periodontal Disease

A 68-year-old female patient with a 15-year history of type 2 diabetes was diagnosed with advanced periodontal disease. Laboratory investigations revealed a fasting blood glucose level of 220 mg/dL and an HbA1c of 9.2%. Clinically, the patient exhibited severe gingival inflammation, deep periodontal pockets measuring 6–7 mm, pronounced gingival recession, and significant alveolar bone loss. Additionally, she had systemic complications, including diabetic nephropathy and retinopathy. The patient was on insulin therapy to stabilize blood glucose levels and reduce advanced glycation end-product (AGE) formation, while adjunct treatment with DPP-4 inhibitors or GLP-1 receptor agonists was introduced due to their anti-inflammatory effects. A multidisciplinary treatment approach was adopted, incorporating flap surgery, bone grafting, and systemic antibiotic therapy with amoxicillin and metronidazole. Anti-inflammatory and antioxidant agents were also utilized to mitigate the disease burden. Over a six-month period, partial reduction in local inflammation was achieved; however, due to long-term uncontrolled diabetes, the structural damage remained largely irreversible.

Case 3: Newly Diagnosed Diabetic Patient with Early Periodontal Changes

A 45-year-old male patient, recently diagnosed with type 2 diabetes, presented with early periodontal changes. His fasting blood glucose was recorded at 170 mg/dL, with an HbA1c of 7.8%. Clinical examination revealed mild gingival inflammation, 3–4 mm periodontal pockets, and initial periodontal changes without significant bone loss. The patient was initiated on metformin for early glycemic control and to mitigate systemic inflammation. A conservative treatment approach was adopted, consisting of professional dental cleaning, oral hygiene education, and low-dose local anti-inflammatory therapy. At the three-month follow-up, the patient's periodontal status remained stable, highlighting the effectiveness of early intervention and systemic metabolic control.

Case 4: Patient Exhibiting an Exaggerated Inflammatory Response

A 55-year-old female patient with a 10-year history of type 2 diabetes exhibited an exaggerated inflammatory response, with fasting blood glucose at 200 mg/dL and an HbA1c of 8.8%. The patient presented with marked gingival inflammation, and laboratory investigations demonstrated elevated levels of pro-inflammatory cytokines, including TNF-α, IL-1β, and IL-6. Periodontal examination revealed 5–6 mm periodontal pockets with significant tissue destruction. Due to the severity of the inflammatory response, biological therapy with anti-TNF agents was considered under a clinical research protocol, while systemic therapy with a GLP-1 receptor agonist was also introduced for its anti-inflammatory properties. Intensive periodontal therapy, including scaling and root planing, root surface debridement, and topical corticosteroids, was implemented. After four months, both systemic and local inflammatory markers showed a reduction, though the long-term efficacy of biological therapy in this context requires further investigation.

Case 5: Young Diabetic Patient – Proactive Management with Rybelsus

A 38-year-old male patient, recently diagnosed with type 2 diabetes, presented with minimal gingival inflammation and early signs of periodontal involvement. His fasting blood glucose was 165 mg/dL, and his HbA1c was 7.5%. Periodontal examination showed slight periodontal pockets and initial gingival recession, while laboratory tests indicated near-normal levels of TNF-α and IL-6. The patient was initiated on Rybelsus, an oral GLP-1 receptor agonist, selected for its ease of administration and potent anti-inflammatory properties. The medication was expected to enhance insulin secretion, reduce blood glucose levels, and modulate pro-inflammatory cytokine release. The patient underwent early periodontal intervention, including professional dental cleaning, comprehensive oral hygiene education, and periodic monitoring. Over a six-month period, treatment with Rybelsus contributed to stable periodontal parameters and the prevention of disease progression, alongside effective systemic glycemic control.

3.1 Comparative Analysis of Antidiabetic Medications on Clinical Outcomes

- Metformin: Demonstrated significant benefits in early-stage patients by reducing systemic inflammation and facilitating periodontal healing.
- Insulin and DPP-4 Inhibitors: Essential for managing advanced or long-standing diabetes; however, their impact on periodontal healing may be moderated by patient age and the extent of tissue damage.
- Rybelsus: Offers distinct advantages due to its oral formulation and robust anti-inflammatory effects. Clinical data suggest that Rybelsus effectively lowers TNF-α and IL-6 levels, thereby contributing to periodontal stability when used in early intervention protocols.

4. Discussion

The presented cases illustrate that periodontal deterioration in diabetic patients is multifactorial, driven by chronic hyperglycemia, systemic inflammation, AGE formation, and immune dysregulation. The increased release of pro-inflammatory cytokines (especially TNF-α, IL-1β, and IL-6) accelerates periodontal breakdown. Effective glycemic control—achieved through medications such as metformin, insulin, and newer agents like Rybelsus—plays a critical role in mitigating these effects.

Rybelsus, in particular, stands out due to its oral administration route and dual benefits in both glycemic regulation and inflammation modulation. The case comparisons indicate that early intervention using Rybelsus may prevent the progression of periodontal disease, making it a promising option in the integrated management of diabetic patients.

The integration of systemic antidiabetic therapy with local periodontal treatment appears crucial. Multidisciplinary approaches combining professional dental care with optimized systemic treatment have shown improved outcomes in terms of reducing local inflammation and stabilizing periodontal parameters.

5. Conclusion

Periodontal health deterioration in diabetic patients results from a complex interplay of chronic hyperglycemia, systemic inflammation, AGE formation, and immune dysfunction. The detailed clinical cases and comprehensive analysis of antidiabetic medications—especially the comparative evaluation of Rybelsus—demonstrate that early diagnosis and multidisciplinary treatment are key to improving periodontal outcomes. Rybelsus, with its potent anti-inflammatory properties and ease of use, represents a significant advancement in the management of diabetes-related periodontal disease. These findings emphasize the need for integrated medical and dental care in diabetic patients, encouraging further research into optimizing periodontal treatment strategies through systemic therapy. Further research should explore long-term comparative trials on GLP-1 receptor agonists like Rybelsus to determine their role in periodontal disease management across diverse diabetic populations.

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