

Microbiome Analysis in Periodontal Disease: Evaluating the Impact of Systemic Medication and Nutritional supplement

Hend A. Alzamil¹, Mubarak N. Alqahtani², Mohammed S. Alanazi³,
Nawaf F. Alharbi⁴, Nada M. Jaber⁵, Hana M. Alsayegh⁶,
Moutaz F. Alluhaydan⁷

Health Affairs at the Ministry of National Guard

Abstract

Periodontal disease is a prevalent condition linked to an imbalance in the oral microbiome, often influenced by systemic medications. This study aimed to evaluate the effects of systemic medications, including antihypertensives, immunosuppressants, and antibiotics, on the composition and diversity of the oral microbiome in patients with periodontal disease. A cross-sectional study was conducted at a tertiary hospital involving 150 patients diagnosed with periodontal disease. The findings revealed that systemic medications significantly altered microbial diversity and increased the prevalence of pathogenic species, contributing to disease progression. Personalized treatment approaches considering systemic medication effects are crucial for effective periodontal disease management. Interdisciplinary collaboration between dentists, pharmacists, and laboratory specialists is essential in developing targeted interventions to mitigate dysbiosis and support oral health.

Keywords: Periodontal Disease, Oral Microbiome, Systemic Medications, Anti hypertensives, Immuno suppressants, Antibiotics, Dysbiosis, Interdisciplinary Collaboration

Introduction

Periodontal disease is a widespread condition affecting millions of people worldwide, characterized by inflammation of the supporting structures of the teeth, potentially leading to tooth loss if left untreated (Kinane et al., 2017). The oral cavity is a complex ecosystem comprising various microbial communities that play a significant role in maintaining oral health. Imbalances in the oral microbiome, often due to lifestyle factors, poor oral hygiene, or systemic influences, can contribute to the pathogenesis of periodontal disease (Lamont & Hajishengallis, 2015). Understanding the intricate relationship between the oral microbiome and systemic influences is essential for improving periodontal disease management.

Systemic medications, including antihypertensives, immunosuppressants, and antibiotics, have been found to significantly alter the oral microbiome, potentially exacerbating periodontal conditions (Slots, 2015). For instance, certain antihypertensive drugs may lead to reduced salivary flow, creating an environment conducive to microbial imbalance (Seki et al., 2020). On the other hand, antibiotics used for treating systemic infections can disrupt microbial equilibrium, affecting both pathogenic and beneficial species

within the oral cavity (Zhang et al., 2015). Despite growing awareness, the precise impact of systemic medications on the oral microbiome and periodontal health remains underexplored.

This study aims to evaluate the influence of systemic medications on the composition and diversity of the oral microbiome in patients with periodontal disease. By combining the expertise of dentists, pharmacists, and laboratory specialists, the study will provide a comprehensive analysis of how systemic medications may contribute to dysbiosis and affect periodontal health. Such insights could pave the way for improved, personalized treatment strategies that account for both local and systemic factors in managing periodontal disease.

Literature Review

The oral microbiome plays a crucial role in maintaining oral health by regulating microbial balance and preventing the overgrowth of pathogenic species. When this balance is disturbed, it can lead to the development of oral diseases, including periodontal disease. Dysbiosis, or an imbalance in the microbial community, is a critical factor in the progression of periodontal disease (Lamont & Hajishengallis, 2015). Research has shown that various systemic factors, such as medications, can influence the oral microbiome, thereby affecting periodontal health (Kinane et al., 2017).

One area of interest is the impact of antihypertensive medications on the oral microbiome. Antihypertensive drugs, particularly those that reduce salivary flow, can lead to a condition known as xerostomia or dry mouth (Seki et al., 2020). Reduced salivary flow impairs the natural cleansing action of saliva, resulting in an environment that favors the growth of pathogenic bacteria. Studies have demonstrated that patients taking antihypertensive medications are at a higher risk of developing periodontal disease due to the resulting microbial imbalance (Seki et al., 2020).

Immunosuppressants, which are commonly prescribed to patients with autoimmune conditions or those undergoing organ transplants, also have a significant impact on the oral microbiome. Immunosuppressive therapy can alter the host immune response, making it difficult for the body to control the growth of pathogenic bacteria in the oral cavity (Slots, 2015). This compromised immune response, combined with changes in the microbial community, can exacerbate periodontal inflammation and increase the risk of periodontal disease.

Antibiotics, while commonly used to treat infections, can also disrupt the oral microbiome by eliminating both pathogenic and beneficial bacterial species (Zhang et al., 2015). The indiscriminate use of antibiotics can lead to a reduction in microbial diversity, which in turn can create an environment that is more susceptible to recolonization by pathogenic bacteria. Studies have shown that long-term or repeated antibiotic use can lead to persistent changes in the oral microbiome, potentially contributing to periodontal disease progression (Zhang et al., 2015).

In addition to medication-induced changes, other systemic factors such as diabetes and hormonal changes have been shown to influence the oral microbiome and contribute to periodontal disease (Kinane et al., 2017). For instance, diabetes is associated with increased levels of glucose in saliva, which can promote the growth of pathogenic bacteria and exacerbate periodontal inflammation. Similarly, hormonal changes during pregnancy or menopause can alter the oral microbiome, increasing the risk of periodontal disease.

Recent advancements in molecular techniques, such as next-generation sequencing, have provided new insights into the complexity of the oral microbiome and its response to systemic medications (Lamont & Hajishengallis, 2015). These technologies have enabled researchers to identify specific changes in microbial composition and diversity associated with different types of systemic medications. By understanding these changes, healthcare providers can develop more targeted interventions to manage periodontal disease in patients taking systemic medications.

The need for interdisciplinary collaboration in managing periodontal disease is increasingly recognized. Dentists, pharmacists, and laboratory specialists each play a crucial role in understanding and mitigating the effects of systemic medications on oral health. Dentists can provide clinical expertise in diagnosing and treating periodontal disease, pharmacists can offer insights into the effects of medications on the oral microbiome, and laboratory specialists can conduct detailed analyses of microbial samples to identify dysbiosis. By working together, these professionals can develop personalized treatment plans that address both local and systemic factors contributing to periodontal disease.

Methodology

This study was conducted in a tertiary hospital setting to evaluate the impact of systemic medications on the oral microbiome in patients with periodontal disease. A cross-sectional study design was used, involving the collaboration of dentists, pharmacists, and laboratory specialists. Ethical approval was obtained from the hospital's ethics committee before commencing the study.

Participants

A total of 150 patients diagnosed with periodontal disease were recruited from the dental department of the tertiary hospital. Participants were selected based on specific inclusion criteria, including adults aged 18 years and older, diagnosed with moderate to severe periodontal disease, and currently taking at least one systemic medication (e.g., antihypertensives, immunosuppressants, or antibiotics). Patients with a history of recent periodontal treatment (within the past 6 months) or those with contraindications to participation were excluded from the study.

Data Collection

Data collection involved clinical examinations, patient interviews, and laboratory analyses. Clinical examinations were performed by experienced dentists to assess the severity of periodontal disease, including measurements of probing depth, clinical attachment level, and bleeding on probing. Patients were interviewed by pharmacists to gather detailed information on their medical history, medication use, and potential side effects, including xerostomia or other oral health complaints.

Saliva and subgingival plaque samples were collected from each participant by the dental team. The laboratory specialists processed these samples to assess the composition and diversity of the oral microbiome. Next-generation sequencing (NGS) was employed to identify and quantify the bacterial species present in the samples. The laboratory analysis focused on identifying shifts in microbial diversity and specific taxa associated with systemic medication use.

Data Analysis

The collected data were analyzed using both descriptive and inferential statistical methods. Clinical data on periodontal health were correlated with microbiome data to determine the relationship between systemic medication use and changes in the oral microbiome. Comparisons were made between patients taking different classes of systemic medications to evaluate their distinct impacts on microbial diversity and periodontal disease severity. Statistical analyses were conducted using SPSS software, with significance set at $p < 0.05$.

Interdisciplinary Collaboration

The interdisciplinary nature of this study was critical in providing a comprehensive understanding of the effects of systemic medications on periodontal health. Dentists contributed their expertise in clinical assessment and diagnosis, pharmacists provided insights into medication use and potential side effects, and laboratory specialists conducted advanced microbial analyses. Regular meetings were held to discuss findings, address challenges, and integrate perspectives from each discipline to ensure a holistic approach to patient care.

Findings

The findings of this study revealed significant associations between systemic medication use and alterations in the oral microbiome among patients with periodontal disease. Specifically, patients using antihypertensive medications showed a marked reduction in salivary flow, which was associated with decreased microbial diversity and an increase in pathogenic species linked to periodontal inflammation (Table 1). Immunosuppressant users also demonstrated reduced microbial diversity and an increased prevalence of specific periodontal pathogens, suggesting a compromised ability to control pathogenic bacteria (Table 2). Antibiotic users, while showing a temporary reduction in pathogenic species, exhibited lower microbial diversity, which can lead to susceptibility to recolonization by opportunistic pathogens (Table 3).

Table 1: Impact of Antihypertensive Medications on Salivary Flow and Microbial Diversity

Parameter	Antihypertensive Users (n=50)	Control Group (n=50)
Salivary Flow Rate (ml/min)	0.45 (± 0.12)	0.75 (± 0.18)
Microbial Diversity Index	1.8 (± 0.3)	2.4 (± 0.4)
Prevalence of Pathogenic Species (%)	68	45

Table 2: Microbial Diversity and Pathogen Prevalence in Immunosuppressant Users

Parameter	Immunosuppressant Users (n=30)	Control Group (n=50)
Microbial Diversity Index	1.6 (± 0.4)	2.4 (± 0.4)
Prevalence of <i>Porphyromonas gingivalis</i> (%)	72	50
Prevalence of <i>Tannerella forsythia</i> (%)	65	40

Table 3: Effects of Antibiotic Use on Microbial Diversity

Parameter	Antibiotic Users (n=70)	Control Group (n=50)
Microbial Diversity Index	1.5 (± 0.3)	2.4 (± 0.4)
Reduction in Pathogenic Species (%)	58	15
Recolonization Rate (%)	70	30

These findings underscore the importance of personalized treatment approaches that consider the impact of systemic medications on the oral microbiome. The reduction in microbial diversity observed in patients taking antihypertensives, immunosuppressants, and antibiotics highlights the need for careful monitoring and potential adjunctive therapies to mitigate dysbiosis and support oral health.

Discussion

The results of this study provide valuable insights into how systemic medications can significantly alter the oral microbiome and impact periodontal health. The findings highlight that systemic medications such as antihypertensives, immunosuppressants, and antibiotics are linked to changes in microbial diversity, which may exacerbate periodontal disease. This supports the hypothesis that systemic medications contribute to dysbiosis, making patients more susceptible to periodontal conditions.

Antihypertensive medications were found to significantly reduce salivary flow, which in turn reduced microbial diversity and increased the prevalence of pathogenic species. These results are consistent with previous studies that identified xerostomia as a key side effect of antihypertensive drugs, leading to an environment that favors pathogenic overgrowth (Seki et al., 2020). The association between reduced salivary flow and periodontal disease severity underscores the importance of addressing dry mouth in patients on antihypertensive therapy, potentially through the use of saliva substitutes or stimulants.

Similarly, the use of immunosuppressants was associated with reduced microbial diversity and an increased prevalence of periodontal pathogens, including *Porphyromonas gingivalis* and *Tannerella forsythia*. Immunosuppressive therapy alters the host immune response, which can impair the body's ability to control pathogenic bacteria, contributing to the progression of periodontal disease (Slots, 2015). These findings suggest that patients on immunosuppressive therapy should be closely monitored for signs of periodontal disease, and preventive measures, such as improved oral hygiene and antimicrobial mouthwashes, should be considered.

The impact of antibiotics on the oral microbiome was also notable. While antibiotics temporarily reduced the prevalence of pathogenic species, they also led to a decrease in overall microbial diversity and a high rate of recolonization by opportunistic pathogens. This aligns with previous research indicating that antibiotics, while effective in managing acute infections, can have long-term consequences on microbial balance (Zhang et al., 2015). The reduction in microbial diversity may increase susceptibility to future infections, highlighting the need for cautious antibiotic use and the potential benefits of probiotic supplementation to restore microbial balance after antibiotic therapy.

These findings emphasize the need for a personalized approach to periodontal disease management, particularly for patients taking systemic medications. Healthcare providers should consider the systemic medications a patient is taking when developing periodontal treatment plans. For instance, strategies to mitigate the side effects of antihypertensives or the immunosuppressive effects of certain medications could

help maintain a healthier oral microbiome. This may include the use of saliva substitutes, antimicrobial agents, and probiotics to support microbial diversity.

The interdisciplinary collaboration between dentists, pharmacists, and laboratory specialists was instrumental in the success of this study. Dentists provided the clinical assessments needed to diagnose and monitor periodontal disease, pharmacists offered crucial insights into the effects of systemic medications, and laboratory specialists conducted detailed analyses of the microbial samples. This collaborative approach allowed for a comprehensive understanding of how systemic medications impact oral health and provided a foundation for developing targeted interventions.

In conclusion, this study highlights the significant impact of systemic medications on the oral microbiome and periodontal health. The reduction in microbial diversity observed among patients taking antihypertensives, immunosuppressants, and antibiotics underscores the importance of personalized treatment strategies that address both local and systemic factors. Further research is needed to explore additional systemic influences on the oral microbiome and to develop effective interventions that can help mitigate these impacts. By integrating the expertise of multiple healthcare disciplines, a more holistic approach to periodontal disease management can be achieved, ultimately improving patient outcomes.

References:

1. Seki, K., Hasuike, A., Iwano, Y., & Hagiwara, Y. (2020). Influence of antihypertensive medications on the clinical parameters of anodized dental implants: a retrospective cohort study. *International Journal of Implant Dentistry*, 6, 1-8.
2. Kinane, D. F., Stathopoulou, P. G., & Papapanou, P. N. (2017). Periodontal diseases. *Nature reviews Disease primers*, 3(1), 1-14.
3. Lamont, R. J., & Hajishengallis, G. (2015). Polymicrobial synergy and dysbiosis in inflammatory disease. *Trends in molecular medicine*, 21(3), 172-183.
4. Zhang, M., Jiang, Z., Li, D., Jiang, D., Wu, Y., Ren, H., ... & Lai, Y. (2015). Oral antibiotic treatment induces skin microbiota dysbiosis and influences wound healing. *Microbial ecology*, 69, 415-421.
5. Slots, J. (2015). Periodontal herpesviruses: prevalence, pathogenicity, systemic risk. *Periodontology* 2000, 69(1), 28-45.

ملخص

مرض اللثة هو حالة شائعة مرتبطة بخلل في ميكروبيوم الفم، وغالبًا ما يتأثر بالأدوية الجهازية. هدفت هذه الدراسة إلى تقييم تأثيرات الأدوية الجهازية، بما في ذلك مضادات ارتفاع ضغط الدم ومثبطات المناعة والمضادات الحيوية، على تكوين وتنوع ميكروبيوم الفم لدى المرضى المصابين بأمراض اللثة. أجريت دراسة مقطعية في مستشفى ثالثي شملت 150 مريضًا تم تشخيصهم بأمراض اللثة. كشفت النتائج أن الأدوية الجهازية غيرت بشكل كبير التنوع الميكروبي وزادت من انتشار الأنواع المسببة للأمراض، مما ساهم في تطور المرض. تعد طرق العلاج

الشخصية مع مراعاة تأثيرات الأدوية الجهازية أمرًا بالغ الأهمية لإدارة أمراض اللثة الفعالة. يعد التعاون متعدد التخصصات بين أطباء الأسنان والصيدلة وأخصائيي المختبرات أمرًا ضروريًا في تطوير التدخلات المستهدفة للتخفيف من خلل التوازن ودعم صحة الفم.

الكلمات الرئيسية: مرض اللثة، ميكروبيوم الفم، الأدوية الجهازية، مضادات ارتفاع ضغط الدم، مثبطات المناعة، المضادات الحيوية، خلل التوازن، التعاون متعدد التخصصات